NOVARTIS

Clinical Trial Results Website

Sponsor

Novartis Pharmaceuticals

Generic Drug Name

GWN323 and PDR001 (spartalizumab)

Trial Indication(s)

Advanced solid tumors and lymphomas

Protocol Number

CGWN323X2101

Protocol Title

A Phase I/Ib open-label, multi-center, dose escalation study of GWN323 (anti-GITR) as a single agent and in combination with PDR001 (anti-PD-1) in patients with advanced solid tumors and lymphomas

Clinical Trial Phase

Phase 1

Phase of Drug Development

Phase 1 GWN323 and phase 3 PDR001.

Study Start/End Dates

Study Start Date: July 2016 (Actual)
Primary Completion Date: March 2020 (Actual)
Study Completion Date: March 2020 (Actual)

Reason for Termination (If applicable)

Due to minimal anti-tumor activity observed, the study was terminated early and the dose expansion part was not initiated. The termination of study GWN323X2101 was not a consequence of any safety concern and has no impact on any other clinical trials involving GWN323 or PDR001.

Study Design/Methodology

This study was a first-in-human, open-label, Phase I/Ib, multi-center study consisting of 2 parts:

- An escalation part with two parallel dose escalations (GWN323 single agent and combination of GWN323 and PDR001).

- An expansion part with parallel enrollment of the single agent and combination treatment arms at their respective recommended doses and schedules.

The maximum dose tested in the escalation phase was sufficient to engage the target, based on the pharmacokinetics modelling data of total receptor occupancy. However, Maximum Tolerated Dose/Recommended dose for expansion (MTD/RDE) was not established. Due to minimal anti-tumor activity observed, the dose expansion part was not initiated. The early study termination was not due to the safety concerns.

In the escalation part of the study, patients were treated for a median time of 9 weeks in the single agent arms and 12 weeks in the combination arms with a maximum duration of treatment of up to 72 weeks and 139 weeks, respectively.

Centers

9 centers in 6 countries: Canada(1), Singapore(1), United States(4), Spain(1), Israel(1), Japan(1)

Objectives:

The primary objective of the trial was to characterize the safety and tolerability of GWN323 as a single agent and in combination with PDR001 and to identify recommended doses and schedules for future studies. The following related endpoints were assessed:

- Incidence of Dose Limiting Toxicities (DLTs) in Cycle 1 (21 days) with single agent GWN323
- Incidence of Dose Limiting Toxicities (DLTs) in Cycle 1 and 2 (42 days) with the combination of GWN323 and PDR001
- Number of participants with dose reductions or interruptions with single agent GWN323 and with the combination of GWN323 and PDR001
- Dose intensity with single agent GWN323 and with the combination of GWN323 and PDR001
- Incidence of adverse events and serious adverse events

The secondary objectives were:

- To assess the preliminary anti-tumor activity of GWN323 as a single agent and in combination with PDR001 in terms of:
  - Number of participants with Best Overall Response (BOR) according to Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST v1.1) and according to immune-related response criteria (irRC)
  - Progression-free survival (PFS)
- To characterize the pharmacokinetics (PK) of GWN323 as a single agent and in combination with PDR001
- To assess the pharmacodynamic effect of GWN323 alone and in combination with PDR001 in tumor samples by measuring the effector/regulatory T cell ratio

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

There were 7 arms of participants treated with single agent GWN323 at the following doses: 10 mg, 30 mg, 60 mg, 150 mg, 375 mg, 750 mg and 1500 mg. In the 7 arms single agent GWN323 was administered via intravenous (i.v.) infusion over 30 minutes every 3 weeks (Q3W). Treatment started on Cycle 1 Day 1 and each cycle consisted of 21 days.

There were 8 arms of participants treated with GWN323 in combination with PDR001 at the following doses: GWN323 10 mg + PDR001 100 mg, GWN323 10 mg + PDR001 200 mg, GWN323 30 mg + PDR001 100 mg, GWN323 30 mg + PDR001 300 mg, GWN323 75 mg + PDR001 300 mg, GWN323 150 mg + PDR001 300 mg, GWN323 300 mg + PDR001 300 mg and GWN323 750 mg + PDR001 300 mg. In the 8 arms GWN323 and PDR001 were administered via i.v. infusion over 30 minutes Q3W. When given in combination, both study drugs were administered separately on the same day with at least 60 minutes break between the two infusions. Treatment started on Cycle 1 Day 1 and each cycle consisted of 21 days.

Statistical Methods

The assessment of safety was based on the type and frequency of adverse events (AEs) as well as on the number of laboratory values that fall outside of pre-determined ranges. Other safety data included electrocardiograms and vital signs.

Evaluation of anti-tumor activity was based on investigator assessment according to RECIST v1.1 and irRC for solid tumors or Cheson 2014 for lymphomas. All analyses were presented using the Full Analysis Set (FAS) that comprised all patients who received at least one full or partial dose of GWN323 or PDR001. Patients were analyzed according to the planned study treatment they had been assigned to. Of note, Progression-Free Survival was not analyzed as Maximum Tolerated Dose/ Recommended dose for expansion (MTD/RDE) could not be established.

Summaries for Best Overall Response were presented as follow:

• RECIST 1.1 and Cheson (2014) together

• irRC and modified Cheson (2014) together

Only PK blood samples with the date and time and for which the last prior dose dates and times were adequately recorded were included in the PK analyses. Missing concentration values were reported as is in data listings. Concentrations below the lower limit of quantification (LLOQ) were treated as zero in summary statistics but handled as missing for the calculation of the geometric means and their coefficient of variation, and reported as is in data listings.

Any missing pharmacokinetic parameter data were not imputed. PK parameters were calculated using non-compartmental methods. Descriptive statistics were presented for all PK parameters by analyte, study arm and study cycle/day.

Study Population: Key Inclusion/Exclusion Criteria

Inclusion Criteria:
- Patients with metastatic and/or advanced solid tumors or lymphomas not amenable to curative treatment by surgery.
- Histologically documented advanced or metastatic solid tumors or lymphomas
- Must have a site of disease amenable to biopsy, and be a candidate for tumor biopsy according to the treating institution's guidelines. Patient must be willing to undergo a new tumor biopsy at screening
-ECOG Performance Status ≤ 2.

Exclusion Criteria:
- Presence of symptomatic central nervous system (CNS) metastases, or CNS metastases that require local CNS-directed therapy (such as radiotherapy or surgery).
- Patients diagnosed with T-cell Lymphomas.
- Patients with prior allogenic transplants.
- Patients previously treated with anti-GITR (Glucocorticoid-Induced TNFR-Related Protein) therapy.
- History of severe hypersensitivity reactions to other monoclonal antibodies.
- Patients intolerant to prior immunotherapy (unable to continue/receive due to immune-related AE).
- Patients with drug-induced pneumonitis, prior or current interstitial lung disease or pneumonitis grade ≥2.

Participant Flow Table

	GWN323 10mg Q3W	GWN323 30mg Q3W	GWN323 60mg Q3W	GWN323 150mg Q3W	GWN323 375mg Q3W	GWN323 750mg Q3W	GWN323 1500mg Q3W
Arm/Group Description	Single agent arm	Single agent arm	Single agent arm	Single agent arm	Single agent arm	Single agent arm	Single agent arm
Started	6	3	5	9	7	5	4
Completed	0	0	0	0	0	0	0
Not Completed	6	3	5	9	7	5	4
Death	0	0	0	0	0	1	0
subject / guardian decision	0	0	1	0	1	0	0
progressive disease	6	3	4	7	6	3	4
Physician Decision	0	0	0	1	0	0	0
Adverse Event	0	0	0	1	0	1	0
Lost to Follow-up	0	0	0	0	0	0	0
study terminated by Sponsor	0	0	0	0	0	0	0

	GWN323 10mg Q3W + PDR001 100mg Q3W	GWN323 10mg Q3W + PDR001 200mg Q3W	GWN323 30mg Q3W + PDR001 100mg Q3W	GWN323 30mg Q3W + PDR001 300mg Q3W	GWN323 75mg Q3W + PDR001 300mg Q3W	GWN323 150mg Q3W + PDR001 300mg Q3W	GWN323 300mg Q3W + PDR001 300mg Q3W	GWN323 750mg Q3W + PDR001 300mg Q3W	Total
Arm/Group Description	Combination arm	Combination arm	Combination arm	Combination arm	Combination arm	Combination arm	Combination arm	Combination arm	
Started	6	4	4	5	5	17	7	5	92
Completed	0	0	0	0	0	0	0	0	0
Not Completed	6	4	4	5	5	17	7	5	92
Death	1	0	0	0	1	0	0	0	3
subject / guardian decision	1	0	0	0	1	1	0	0	5
progressive disease	4	3	3	4	2	15	6	4	74
Physician Decision	0	0	0	0	0	0	1	1	3
Adverse Event	0	1	1	0	0	0	0	0	4
Lost to Follow-up	0	0	0	0	1	0	0	0	1
study terminated by Sponsor	0	0	0	1	0	1	0	0	2

Baseline Characteristics

	GWN323 10mg Q3W	GWN323 30mg Q3W	GWN323 60mg Q3W	GWN323 150mg Q3W	GWN323 375mg Q3W	GWN323 750mg Q3W	GWN323 1500mg Q3W
Arm/Group Description	Single agent arm	Single agent arm	Single agent arm	Single agent arm	Single agent arm	Single agent arm	Single agent arm
Number of Participants [units: participants]	6	3	5	9	7	5	4
Age Continuous (units: years) Mean ± Standard Deviation							
	61.5±6.19	51.3±19.55	67.2±12.07	55.6±6.97	59.7±8.62	58.4±15.79	70.5±10.21
Sex: Female, Male (units: participants) Count of Participants (Not Applicable)							
Female	3	2	3	4	4	3	3
Male	3	1	2	5	3	2	1
Race/Ethnicity, Customized (units: participants) Count of Participants (Not Applicable)							
White	4	2	4	6	2	3	3
Asian	1	1	1	3	3	1	0
Other	1	0	0	0	0	1	0
Unknown	0	0	0	0	1	0	1
Black or African American	0	0	0	0	1	0	0

	GWN323 10mg Q3W + PDR001 100mg Q3W	GWN323 10mg Q3W + PDR001 200mg Q3W	GWN323 30mg Q3W + PDR001 100mg Q3W	GWN323 30mg Q3W + PDR001 300mg Q3W	GWN323 75mg Q3W + PDR001 300mg Q3W	GWN323 150mg Q3W + PDR001 300mg Q3W	GWN323 300mg Q3W + PDR001 300mg Q3W	GWN323 750mg Q3W + PDR001 300mg Q3W	Total
Arm/Group Description	Combination arm	Combination arm	Combination arm	Combination arm	Combination arm	Combination arm	Combination arm	Combination arm	
Number of Participants [units: participants]	6	4	4	5	5	17	7	5	92
Age Continuous (units: years) Mean ± Standard Deviation									
	54.7±11.11	65.0±10.86	53.3±11.15	55.6±12.86	64.4±8.26	61.2±12.77	59.6±13.72	55.4±7.27	59.6±11.4
Sex: Female, Male (units: participants) Count of Participants (Not Applicable)									
Female	3	2	1	0	2	9	4	2	45
Male	3	2	3	5	3	8	3	3	47
Race/Ethnicity, Customized (units: participants) Count of Participants (Not Applicable)									
White	4	4	3	4	2	14	2	3	60
Asian	2	0	1	1	1	2	2	1	20
Other	0	0	0	0	0	0	1	0	3
Unknown	0	0	0	0	0	1	1	1	5
Black or African American	0	0	0	0	2	0	1	0	4

Primary Outcome Result(s)

Incidence of Dose Limiting Toxicities (DLTs) in Cycle 1 (21 days) with single agent GWN323

(Time Frame: 21 days)

	GWN323 10mg Q3W	GWN323 30mg Q3W	GWN323 60mg Q3W	GWN323 150mg Q3W	GWN323 375mg Q3W	GWN323 750mg Q3W	GWN323 1500mg Q3W
Arm/Group Description	Single agent arm	Single agent arm	Single agent arm	Single agent arm	Single agent arm	Single agent arm	Single agent arm
Number of Participants Analyzed	6	3	5	8	7	5	4
Incidence of Dose Limiting Toxicities (DLTs) in Cycle 1 (21 days) with single agent GWN323 (units: participants) Count of Participants (Not Applicable)							
	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)

Incidence of Dose Limiting Toxicities (DLTs) in Cycle 1 and 2 (42 days) with the combination of GWN323 and PDR001

(Time Frame: 42 days)

	GWN323 10mg Q3W + PDR001 100mg Q3W	GWN323 10mg Q3W + PDR001 200mg Q3W	GWN323 30mg Q3W + PDR001 100mg Q3W	GWN323 30mg Q3W + PDR001 300mg Q3W	GWN323 75mg Q3W + PDR001 300mg Q3W	GWN323 150mg Q3W + PDR001 300mg Q3W	GWN323 300mg Q3W + PDR001 300mg Q3W	GWN323 750mg Q3W + PDR001 300mg Q3W
Arm/Group Description	Combination arm	Combination arm	Combination arm	Combination arm	Combination arm	Combination arm	Combination arm	Combination arm
Number of Participants Analyzed	6	4	4	5	4	17	7	3
Incidence of Dose Limiting Toxicities (DLTs) in Cycle 1 and 2 (42 days) with the combination of GWN323 and PDR001 (units: participants) Count of Participants (Not Applicable)								
	0 (%)	1 (25%)	1 (25%)	0 (%)	0 (%)	1 (5.88%)	0 (%)	0 (%)

Number of participants with dose reductions or interruptions with single agent GWN323

(Time Frame: 9 weeks median, up to 72 weeks)

	GWN323 10mg Q3W	GWN323 30mg Q3W	GWN323 60mg Q3W	GWN323 150mg Q3W	GWN323 375mg Q3W	GWN323 750mg Q3W	GWN323 1500mg Q3W
Arm/Group Description	Single agent arm	Single agent arm	Single agent arm	Single agent arm	Single agent arm	Single agent arm	Single agent arm
Number of Participants Analyzed	6	3	5	9	7	5	4
Number of participants with dose reductions or interruptions with single agent GWN323 (units: participants) Count of Participants (Not Applicable)							
	1 (16.67%)	0 (%)	0 (%)	0 (%)	0 (%)	1 (20%)	0 (%)

Number of participants with dose reductions or interruptions with the combination of GWN323 and PDR001

(Time Frame: 12 weeks median, up to 139 weeks)

	GWN323 10mg Q3W + PDR001 100mg Q3W	GWN323 10mg Q3W + PDR001 200mg Q3W	GWN323 30mg Q3W + PDR001 100mg Q3W	GWN323 30mg Q3W + PDR001 300mg Q3W	GWN323 75mg Q3W + PDR001 300mg Q3W	GWN323 150mg Q3W + PDR001 300mg Q3W	GWN323 300mg Q3W + PDR001 300mg Q3W	GWN323 750mg Q3W + PDR001 300mg Q3W
Arm/Group Description	Combination arm	Combination arm	Combination arm	Combination arm	Combination arm	Combination arm	Combination arm	Combination arm
Number of Participants Analyzed	6	4	4	5	5	17	7	5
Number of participants with dose reductions or interruptions with the combination of GWN323 and PDR001 (units: participants) Count of Participants (Not Applicable)								
Dose reductions or interruptions of GWN323	0 (%)	0 (%)	1 (25%)	0 (%)	1 (20%)	4 (23.53%)	0 (%)	1 (20%)
Dose reductions or interruptions of PRD001	0 (%)	0 (%)	1 (25%)	0 (%)	1 (20%)	3 (17.65%)	0 (%)	1 (20%)

Dose intensity with single agent GWN323

(Time Frame: 9 weeks median, up to 72 weeks)

	GWN323 10mg Q3W	GWN323 30mg Q3W	GWN323 60mg Q3W	GWN323 150mg Q3W	GWN323 375mg Q3W	GWN323 750mg Q3W	GWN323 1500mg Q3W
Arm/Group Description	Single agent arm	Single agent arm	Single agent arm	Single agent arm	Single agent arm	Single agent arm	Single agent arm
Number of Participants Analyzed	6	3	5	9	7	5	4
Dose intensity with single agent GWN323 (units: mg/week) Mean ± Standard Deviation							
	13.1 ± 22.47	10.1 ± 0.09	19.9 ± 0.21	51.6 ± 4.61	124.9 ± 0.2	237.7 ± 18.42	487.2 ± 25.64

Dose intensity with the combination of GWN323 and PDR001

(Time Frame: 12 weeks median, up to 139 weeks)

	GWN323 10mg Q3W + PDR001 100mg Q3W	GWN323 10mg Q3W + PDR001 200mg Q3W	GWN323 30mg Q3W + PDR001 100mg Q3W	GWN323 30mg Q3W + PDR001 300mg Q3W	GWN323 75mg Q3W + PDR001 300mg Q3W	GWN323 150mg Q3W + PDR001 300mg Q3W	GWN323 300mg Q3W + PDR001 300mg Q3W	GWN323 750mg Q3W + PDR001 300mg Q3W
Arm/Group Description	Combination arm	Combination arm	Combination arm	Combination arm	Combination arm	Combination arm	Combination arm	Combination arm
Number of Participants Analyzed	6	4	4	5	5	17	7	5
Dose intensity with the combination of GWN323 and PDR001 (units: mg/week) Mean ± Standard Deviation								
Dose intensity of GWN323	3.2 ± 0.60	3.1 ± 0.37	17.7 ± 15.32	14.2 ± 8.73	20 ± 3.2	45.5 ± 8.58	98.6 ± 2.1	242.2 ± 26.63
Dose intensity of PRD001	34 ± 8.91	62.7 ± 7.41	42.7 ± 18.82	93.1 ± 9.65	82.3 ± 13	93.6 ± 12.15	98.6 ± 2.1	96.9 ± 10.65

Secondary Outcome Result(s)

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

(Time Frame: From first dose of study treatment up to 76 weeks (single agent arms) and up to 143 weeks (combination arms))

	GWN323 10mg Q3W	GWN323 30mg Q3W	GWN323 60mg Q3W	GWN323 150mg Q3W	GWN323 375mg Q3W	GWN323 750mg Q3W	GWN323 1500mg Q3W
Arm/Group Description	Single agent arm	Single agent arm	Single agent arm	Single agent arm	Single agent arm	Single agent arm	Single agent arm
Number of Participants Analyzed	6	3	5	9	7	5	4
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 (%)
Partial Response (PR)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)
Stable Disease (SD)	3 (50%)	0 (%)	0 (%)	2 (22.22%)	1 (14.29%)	1 (20%)	0 (%)
Progressive disease (PD)	3 (50%)	2 (66.67%)	5 (100%)	6 (66.67%)	5 (71.43%)	3 (60%)	2 (50%)
Unknown	0 (%)	1 (33.33%)	0 (%)	1 (11.11%)	1 (14.29%)	1 (20%)	2 (50%)

	GWN323 10mg Q3W + PDR001 100mg Q3W	GWN323 10mg Q3W + PDR001 200mg Q3W	GWN323 30mg Q3W + PDR001 100mg Q3W	GWN323 30mg Q3W + PDR001 300mg Q3W	GWN323 75mg Q3W + PDR001 300mg Q3W	GWN323 150mg Q3W + PDR001 300mg Q3W	GWN323 300mg Q3W + PDR001 300mg Q3W	GWN323 750mg Q3W + PDR001 300mg Q3W
Arm/Group Description	Combination arm	Combination arm	Combination arm	Combination arm	Combination arm	Combination arm	Combination arm	Combination arm
Number of Participants Analyzed	6	4	4	5	5	17	7	5
Number of participants with Best Overall Response (BOR) per RECIST 1.1 (units: participants) Count of Participants (Not Applicable)								
Complete Response (CR)	1 (16.67%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)
Partial Response (PR)	0 (%)	0 (%)	0 (%)	1 (20%)	0 (%)	2 (11.76%)	0 (%)	0 (%)
Stable Disease (SD)	1 (16.67%)	2 (50%)	2 (50%)	1 (20%)	2 (40%)	4 (23.53%)	1 (14.29%)	1 (20%)
Progressive disease (PD)	3 (50%)	1 (25%)	1 (25%)	3 (60%)	2 (40%)	11 (64.71%)	4 (57.14%)	2 (40%)
Unknown	1 (16.67%)	1 (25%)	1 (25%)	0 (%)	1 (20%)	0 (%)	2 (28.57%)	2 (40%)

Number of participants with Best Overall Response (BOR) per IrRC

(Time Frame: From first dose of study treatment up to 76 weeks (single agent arms) and up to 143 weeks (combination arms))

	GWN323 10mg Q3W	GWN323 30mg Q3W	GWN323 60mg Q3W	GWN323 150mg Q3W	GWN323 375mg Q3W	GWN323 750mg Q3W	GWN323 1500mg Q3W
Arm/Group Description	Single agent arm	Single agent arm	Single agent arm	Single agent arm	Single agent arm	Single agent arm	Single agent arm
Number of Participants Analyzed	6	3	5	9	7	5	4
Number of participants with Best Overall Response (BOR) per IrRC (units: participants) Count of Participants (Not Applicable)							
Complete Response (CR)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)
Partial Response (PR)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)
Stable Disease (SD)	3 (50%)	0 (%)	0 (%)	2 (22.22%)	1 (14.29%)	1 (20%)	0 (%)
Progressive disease (PD)	3 (50%)	2 (66.67%)	5 (100%)	6 (66.67%)	5 (71.43%)	3 (60%)	2 (50%)
Unknown	0 (%)	1 (33.33%)	0 (%)	1 (11.11%)	1 (14.29%)	1 (20%)	2 (50%)

	GWN323 10mg Q3W + PDR001 100mg Q3W	GWN323 10mg Q3W + PDR001 200mg Q3W	GWN323 30mg Q3W + PDR001 100mg Q3W	GWN323 30mg Q3W + PDR001 300mg Q3W	GWN323 75mg Q3W + PDR001 300mg Q3W	GWN323 150mg Q3W + PDR001 300mg Q3W	GWN323 300mg Q3W + PDR001 300mg Q3W	GWN323 750mg Q3W + PDR001 300mg Q3W
Arm/Group Description	Combination arm	Combination arm	Combination arm	Combination arm	Combination arm	Combination arm	Combination arm	Combination arm
Number of Participants Analyzed	6	4	4	5	5	17	7	5
Number of participants with Best Overall Response (BOR) per IrRC (units: participants) Count of Participants (Not Applicable)								
Complete Response (CR)	1 (16.67%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)
Partial Response (PR)	0 (%)	0 (%)	0 (%)	1 (20%)	0 (%)	2 (11.76%)	0 (%)	0 (%)
Stable Disease (SD)	1 (16.67%)	2 (50%)	2 (50%)	1 (20%)	2 (40%)	4 (23.53%)	1 (14.29%)	1 (20%)
Progressive disease (PD)	3 (50%)	1 (25%)	1 (25%)	3 (60%)	2 (40%)	11 (64.71%)	4 (57.14%)	2 (40%)
Unknown	1 (16.67%)	1 (25%)	1 (25%)	0 (%)	1 (20%)	0 (%)	2 (28.57%)	2 (40%)

Progression-Free Survival (PFS)

(Time Frame: From date of start of treatment up to the date of event defined as the first documented progression or death due to any cause.)

PFS was to be analyzed at Maximum Tolerated Dose/ Recommended dose for expansion (MTD/RDE). As MTD/RDE was not established, PFS was not analyzed.

Maximum observed serum concentration (Cmax) of GWN323

(Time Frame: End of intravenous infusion (± 5 minutes))

	GWN323 10mg Q3W	GWN323 30mg Q3W	GWN323 60mg Q3W	GWN323 150mg Q3W	GWN323 375mg Q3W	GWN323 750mg Q3W	GWN323 1500mg Q3W
Arm/Group Description	Single agent arm	Single agent arm	Single agent arm	Single agent arm	Single agent arm	Single agent arm	Single agent arm
Number of Participants Analyzed	6 (C1D1) 5 (C4D1)	3 (C1D1) 0 (C4D1)	5 (C1D1) 3 (C4D1)	6 (C1D1) 2 (C4D1)	3 (C1D1) 0 (C4D1)	5 (C1D1) 1 (C4D1)	4 (C1D1) 2 (C4D1)
Maximum observed serum concentration (Cmax) of GWN323 (units: ng/mL) Geometric Mean (Geometric Coefficient of Variation)							
Cmax, Cycle 1 Day 1 (C1D1)	4880 (54.3%)	8820 (43.5%)	19300 (31.5%)	36500 (27.8%)	123000 (32.6%)	247000 (8.6%)	438000 (47.6%)
Cmax, Cycle 4 Day 1 (C4D1)	6450 (30.3%)	N/A	25200 (17.9%)	51800 (11.6%)	N/A	304000 (–)	668000 (44.9%)

N/A: No participants with evaluable PK parameters.

	GWN323 10mg Q3W + PDR001 100mg Q3W	GWN323 10mg Q3W + PDR001 200mg Q3W	GWN323 30mg Q3W + PDR001 100mg Q3W	GWN323 30mg Q3W + PDR001 300mg Q3W	GWN323 75mg Q3W + PDR001 300mg Q3W	GWN323 150mg Q3W + PDR001 300mg Q3W	GWN323 300mg Q3W + PDR001 300mg Q3W	GWN323 750mg Q3W + PDR001 300mg Q3W
Arm/Group Description	Combination arm	Combination arm	Combination arm	Combination arm	Combination arm	Combination arm	Combination arm	Combination arm
Number of Participants Analyzed	5 (C1D1) 3 (C4D1)	4 (C1D1) 2 (C4D1)	3 (C1D1) 3 (C4D1)	4 (C1D1) 3 (C4D1)	4 (C1D1) 2 (C4D1)	5 (C1D1) 2 (C4D1)	4 (C1D1) 0 (C4D1)	0 (C1D1) 0 (C4D1)
Maximum observed serum concentration (Cmax) of GWN323 (units: ng/mL) Geometric Mean (Geometric Coefficient of Variation)								
Cmax, Cycle 1 Day 1 (C1D1)	2650 (20.3%)	2550 (39.3%)	7190 (15.5%)	8090 (27.1%)	22900 (37.5%)	37000 (40.1%)	104000 (36.2%)	N/A
Cmax, Cycle 4 Day 1 (C4D1)	2700 (47.1%)	5490 (46.4%)	10100 (34.4%)	10500 (18.8%)	58800 (28.1%)	46900 (28.1%)	N/A	N/A

N/A: No participants with evaluable PK parameters.

Area under the serum concentration-time curve from time zero to the time of last quantifiable concentration point (AUClast) of GWN323

(Time Frame: Pre-dose, end of infusion (± 5 minutes), 24, 72, 168 and 336 hours post-infusion administered on Day 1 of Cycle 1 and Cycle 4)

	GWN323 10mg Q3W	GWN323 30mg Q3W	GWN323 60mg Q3W	GWN323 150mg Q3W	GWN323 375mg Q3W	GWN323 750mg Q3W	GWN323 1500mg Q3W
Arm/Group Description	Single agent arm	Single agent arm	Single agent arm	Single agent arm	Single agent arm	Single agent arm	Single agent arm
Number of Participants Analyzed	6 (C1D1) 5 (C4D1)	2 (C1D1) 0 (C4D1)	5 (C1D1) 3 (C4D1)	6 (C1D1) 2 (C4D1)	3 (C1D1) 0 (C4D1)	4 (C1D1) 1 (C4D1)	4 (C1D1) 2 (C4D1)
Area under the serum concentration-time curve from time zero to the time of last quantifiable concentration point (AUClast) of GWN323 (units: h*ng/mL) Geometric Mean (Geometric Coefficient of Variation)							
AUClast, Cycle 1 Day 1 (C1D1)	630000 (38.8%)	1810000 (22.6%)	3680000 (31.8%)	5360000 (42.3%)	14400000 (34.8%)	41800000 (34.8%)	77100000 (45.9%)
AUClast, Cycle 4 Day 1 (C4D1)	1310000 (52.1%)	N/A	4820000 (48.8%)	11800000 (39.1%)	N/A	102000000 (–)	113000000 (26.3%)

N/A: No participants with evaluable PK parameters.

	GWN323 10mg Q3W + PDR001 100mg Q3W	GWN323 10mg Q3W + PDR001 200mg Q3W	GWN323 30mg Q3W + PDR001 100mg Q3W	GWN323 30mg Q3W + PDR001 300mg Q3W	GWN323 75mg Q3W + PDR001 300mg Q3W	GWN323 150mg Q3W + PDR001 300mg Q3W	GWN323 300mg Q3W + PDR001 300mg Q3W	GWN323 750mg Q3W + PDR001 300mg Q3W
Arm/Group Description	Combination arm	Combination arm	Combination arm	Combination arm	Combination arm	Combination arm	Combination arm	Combination arm
Number of Participants Analyzed	5 (C1D1) 3 (C4D1)	4 (C1D1) 2 (C4D1)	3 (C1D1) 3 (C4D1)	4 (C1D1) 3 (C4D1)	4 (C1D1) 2 (C4D1)	5 (C1D1) 1 (C4D1)	3 (C1D1) 0 (C4D1)	0 (C1D1) 0 (C4D1)
Area under the serum concentration-time curve from time zero to the time of last quantifiable concentration point (AUClast) of GWN323 (units: h*ng/mL) Geometric Mean (Geometric Coefficient of Variation)								
AUClast, Cycle 1 Day 1 (C1D1)	385000 (26.3%)	491000 (43.9%)	1100000 (64.6%)	1290000 (21.5%)	4700000 (32.7%)	6400000 (34.8%)	22100000 (45.8%)	N/A
AUClast, Cycle 4 Day 1 (C4D1)	771000 (82.4%)	2090000 (38.7%)	3310000 (67.7%)	2470000 (14.6%)	28000000 (101.2%)	15300000 (–)	N/A	N/A

N/A: No participants with evaluable PK parameters.

Number of participants with anti-GWN323 antibodies

(Time Frame: From pre-dose (baseline) up to 76 weeks (single agent arms) and up to 143 weeks (combination arms))

	GWN323 10mg Q3W	GWN323 30mg Q3W	GWN323 60mg Q3W	GWN323 150mg Q3W	GWN323 375mg Q3W	GWN323 750mg Q3W	GWN323 1500mg Q3W
Arm/Group Description	Single agent arm	Single agent arm	Single agent arm	Single agent arm	Single agent arm	Single agent arm	Single agent arm
Number of Participants Analyzed	6	3	5	6	4	3	4
Number of participants with anti-GWN323 antibodies (units: participants) Count of Participants (Not Applicable)							
ADA-positive at baseline	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)
Treatment-induced ADA-positive	1 (16.67%)	1 (33.33%)	1 (20%)	3 (50%)	0 (%)	0 (%)	0 (%)

	GWN323 10mg Q3W + PDR001 100mg Q3W	GWN323 10mg Q3W + PDR001 200mg Q3W	GWN323 30mg Q3W + PDR001 100mg Q3W	GWN323 30mg Q3W + PDR001 300mg Q3W	GWN323 75mg Q3W + PDR001 300mg Q3W	GWN323 150mg Q3W + PDR001 300mg Q3W	GWN323 300mg Q3W + PDR001 300mg Q3W	GWN323 750mg Q3W + PDR001 300mg Q3W
Arm/Group Description	Combination arm	Combination arm	Combination arm	Combination arm	Combination arm	Combination arm	Combination arm	Combination arm
Number of Participants Analyzed	6	4	3	5	5	15	6	4
Number of participants with anti-GWN323 antibodies (units: participants) Count of Participants (Not Applicable)								
ADA-negative at baseline	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	1 (6.67%)	0 (%)	1 (25%)
Treatment-induced ADA-positive	0 (%)	1 (25%)	0 (%)	1 (20%)	2 (40%)	1 (7.14%)	0 (%)	0 (%)

Number of participants with anti-PDR001 antibodies

(Time Frame: From pre-dose (baseline) up to 76 weeks (single agent arms) and up to 143 weeks (combination arms))

This endpoint was not analyzed because this is an early terminated study. Due to minimal anti-tumor activity observed, the dose expansion part was not initiated and the study lacked sufficient data to support this outcome measure.

Effector/regulatory T cell ratio

(Time Frame: Baseline, Cycle 2 Day 1, Cycle 4 Day 1)

	GWN323 10mg Q3W	GWN323 30mg Q3W	GWN323 60mg Q3W	GWN323 150mg Q3W	GWN323 375mg Q3W	GWN323 750mg Q3W	GWN323 1500mg Q3W
Arm/Group Description	Single agent arm	Single agent arm	Single agent arm	Single agent arm	Single agent arm	Single agent arm	Single agent arm
Number of Participants Analyzed	6 (Baseline) 6 (C2D1) 1 (C4D1)	3 (Baseline) 3 (C2D1) 0 (C4D1)	4 (Baseline) 3 (C2D1) 0 (C4D1)	8 (Baseline) 2 (C2D1) 0 (C4D1)	6 (Baseline) 3 (C2D1) 0 (C4D1)	5 (Baseline) 4 (C2D1) 0 (C4D1)	4 (Baseline) 3 (C2D1) 0 (C4D1)
Effector/regulatory T cell ratio (units: no units) Median (Full Range)							
Baseline	4.8 (0 to 28)	3.1 (2 to 18)	6.2 (2 to 50)	6.9 (1 to 37)	4.1 (2 to 8)	1.8 (1 to 3)	5.6 (2 to 26)
Cycle 2 Day 1 (C2D1)	3.8 (3 to 10)	2.1 (2 to 8)	6.0 (3 to 17)	8.3 (2 to 15)	8.0 (1 to 8)	2.6 (2 to 3)	13.7 (5 to 14)
Cycle 4 Day 1 (C4D1)	45.7 (46 to 46)	N/A	N/A	N/A	N/A	N/A	N/A

N/A: No participants with evaluable T cell measurements.

	GWN323 10mg Q3W + PDR001 100mg Q3W	GWN323 10mg Q3W + PDR001 200mg Q3W	GWN323 30mg Q3W + PDR001 100mg Q3W	GWN323 30mg Q3W + PDR001 300mg Q3W	GWN323 75mg Q3W + PDR001 300mg Q3W	GWN323 150mg Q3W + PDR001 300mg Q3W	GWN323 300mg Q3W + PDR001 300mg Q3W	GWN323 750mg Q3W + PDR001 300mg Q3W
Arm/Group Description	Combination arm	Combination arm	Combination arm	Combination arm	Combination arm	Combination arm	Combination arm	Combination arm
Number of Participants Analyzed	6 (Baseline) 6 (C2D1) 0 (C4D1)	2 (Baseline) 3 (C2D1) 0 (C4D1)	3 (Baseline) 3 (C2D1) 0 (C4D1)	3 (Baseline) 5 (C2D1) 0 (C4D1)	5 (Baseline) 2 (C2D1) 0 (C4D1)	14 (Baseline) 10 (C2D1) 1 (C4D1)	6 (Baseline) 4 (C2D1) 0 (C4D1)	3 (Baseline) 4 (C2D1) 0 (C4D1)
Baseline	7.0 (2 to 22)	23.3 (6 to 41)	6.5 (2 to 9)	19.8 (5 to 22)	4.7 (1 to 11)	3.4 (1 to 26)	10.9 (4 to 289)	6.9 (3 to 8)
Cycle 2 Day 1 (C2D1)	10.2 (2 to 40)	12.0 (3 to 15)	10.0 (4 to 19)	7.0 (1 to 13)	2.4 (2 to 3)	3.9 (2 to 17)	8.1 (1 to 2424)	3.7 (2 to 23)
Cycle 4 Day 1 (C4D1)	N/A	N/A	N/A	N/A	N/A	6.0 (6 to 6)	N/A	N/A

N/A: No participants with evaluable T cell measurements.

Safety Results

All-Cause Mortality

	GWN323 10mg Q3W N = 6	GWN323 30mg Q3W N = 3	GWN323 60mg Q3W N = 5	GWN323 150mg Q3W N = 9	GWN323 375mg Q3W N = 7	GWN323 750mg Q3W N = 5	GWN323 1500mg Q3W N = 4
Arm/Group Description	Single agent arm	Single agent arm	Single agent arm	Single agent arm	Single agent arms	Single agent arm	Single agent arm
Total participants affected	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

	GWN323 10mg Q3W + PDR001 100mg Q3W N = 6	GWN323 10mg Q3W + PDR001 200mg Q3W N = 4	GWN323 30mg Q3W + PDR001 100mg Q3W N = 4	GWN323 30mg Q3W + PDR001 300mg Q3W N = 5	GWN323 75mg Q3W + PDR001 300mg Q3W N = 5	GWN323 150mg Q3W + PDR001 300mg Q3W N = 17	GWN323 300mg Q3W + PDR001 300mg Q3W N = 7	GWN323 750mg Q3W + PDR001 300mg Q3W N = 5
Arm/Group Description	Combination arm	Combination arm	Combination arm	Combination arm	Combination arm	Combination arm	Combination arm	Combination arm
Total participants affected	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Serious Adverse Events by System Organ Class

Time Frame	From first dose of study treatment until last dose plus 30 days, up to maximum duration of 76 weeks (single agent arms) and up to 143 weeks (combination arms).
Additional Description	Any sign or symptom that occurs during the study treatment plus the 30 days post treatment.
Source Vocabulary for Table Default	MedDRA (23.0)
Assessment Type for Table Default	Systematic Assessment

	GWN323 10mg Q3W N = 6	GWN323 30mg Q3W N = 3	GWN323 60mg Q3W N = 5	GWN323 150mg Q3W N = 9	GWN323 375mg Q3W N = 7	GWN323 750mg Q3W N = 5	GWN323 1500mg Q3W N = 4
Arm/Group Description	Single agent arm	Single agent arm	Single agent arm	Single agent arm	Single agent arms	Single agent arm	Single agent arm
Total participants affected	2 (33.33%)	2 (66.67%)	0 (0.00%)	3 (33.33%)	2 (28.57%)	2 (40.00%)	1 (25.00%)
Blood and lymphatic system disorders							
Anaemia	0 (0.00%)	2 (66.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Gastrointestinal disorders							
Abdominal pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)
Constipation	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)
Gastric haemorrhage	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Gastrointestinal haemorrhage	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Large intestinal obstruction	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	0 (0.00%)
Nausea	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	1 (25.00%)
Small intestinal obstruction	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)
Vomiting	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	1 (25.00%)
General disorders and administration site conditions							
Fatigue	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hepatobiliary disorders							
Bile duct obstruction	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Cholangitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Infections and infestations							
Cellulitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pneumonia	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Sepsis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Skin infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Upper respiratory tract infection	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Injury, poisoning and procedural complications							
Foot fracture	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Infusion related reaction	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Stoma obstruction	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Urinary tract stoma complication	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Investigations							
Blood bilirubin increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Metabolism and nutrition disorders							
Decreased appetite	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)
Dehydration	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)
Hyperkalaemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hyponatraemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	0 (0.00%)
Musculoskeletal and connective tissue disorders							
Back pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Neck pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)							
Tumour pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	0 (0.00%)
Nervous system disorders							
Seizure	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Psychiatric disorders							
Hallucination	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	0 (0.00%)
Renal and urinary disorders							
Acute kidney injury	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Anuria	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Obstructive nephropathy	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Renal impairment	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Respiratory, thoracic and mediastinal disorders							
Cough	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)
Dyspnoea	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)
Painful respiration	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pleuritic pain	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pulmonary embolism	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	1 (20.00%)	0 (0.00%)
Respiratory failure	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Vascular disorders							
Hypotension	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

	GWN323 10mg Q3W + PDR001 100mg Q3W N = 6	GWN323 10mg Q3W + PDR001 200mg Q3W N = 4	GWN323 30mg Q3W + PDR001 100mg Q3W N = 4	GWN323 30mg Q3W + PDR001 300mg Q3W N = 5	GWN323 75mg Q3W + PDR001 300mg Q3W N = 5	GWN323 150mg Q3W + PDR001 300mg Q3W N = 17	GWN323 300mg Q3W + PDR001 300mg Q3W N = 7	GWN323 750mg Q3W + PDR001 300mg Q3W N = 5
Arm/Group Description	Combination arm	Combination arm	Combination arm	Combination arm	Combination arm	Combination arm	Combination arm	Combination arm
Total participants affected	3 (50.00%)	0 (0.00%)	3 (75.00%)	1 (20.00%)	3 (60.00%)	4 (23.53%)	2 (28.57%)	2 (40.00%)
Blood and lymphatic system disorders								
Anaemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Gastrointestinal disorders								
Abdominal pain	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)	0 (0.00%)	1 (20.00%)
Constipation	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Gastric haemorrhage	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)
Gastrointesti-nal haemorrhage	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Large intestinal obstruction	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Nausea	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)
Small intestinal obstruction	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)	0 (0.00%)	0 (0.00%)
Vomiting	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)	1 (14.29%)	0 (0.00%)

General disorders and administration site conditions								
Fatigue	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hepatobiliary disorders								
Bile duct obstruction	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Cholangitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Infections and infestations								
Cellulitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pneumonia	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Sepsis	1 (16.67%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Skin infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)	0 (0.00%)	0 (0.00%)
Upper 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%)
Injury, poisoning and procedural complications								
Foot fracture	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Infusion related reaction	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)	0 (0.00%)	0 (0.00%)
Stoma obstruction	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Urinary tract stoma complication	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)
Investigations								

Blood bilirubin increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Metabolism and nutrition disorders								
Decreased appetite	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Dehydration	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)
Hyperkalaemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hyponatraemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Musculoskeletal and connective tissue disorders								
Back pain	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Neck 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%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)								
Tumour 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%)
Nervous system disorders								
Seizure	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Psychiatric disorders								
Hallucination	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
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%)
Anuria	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Obstructive nephropathy	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)

Renal impairment	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Respiratory, thoracic and mediastinal disorders								
Cough	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Dyspnoea	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Painful respiration	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pleuritic 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%)
Pulmonary embolism	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Respiratory failure	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Vascular disorders								
Hypotension	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)

Other Adverse Events by System Organ Class

Time Frame	From first dose of study treatment until last dose plus 30 days, up to maximum duration of 76 weeks (single agent arms) and up to 143 weeks (combination arms).
Additional Description	Any sign or symptom that occurs during the study treatment plus the 30 days post treatment.
Source Vocabulary for Table Default	MedDRA (23.0)
Assessment Type for Table Default	Systematic Assessment
Frequent Event Reporting Threshold	5%

	GWN323 10mg Q3W N = 6	GWN323 30mg Q3W N = 3	GWN323 60mg Q3W N = 5	GWN323 150mg Q3W N = 9	GWN323 375mg Q3W N = 7	GWN323 750mg Q3W N = 5	GWN323 1500mg Q3W N = 4
Arm/Group Description	Single agent arm	Single agent arm	Single agent arm	Single agent arm	Single agent arms	Single agent arm	Single agent arm
Total participants affected	6 (100.00%)	3 (100.00%)	5 (100.00%)	8 (88.89%)	7 (100.00%)	5 (100.00%)	4 (100.00%)
Blood and lymphatic system disorders							
Anaemia	0 (0.00%)	2 (66.67%)	0 (0.00%)	2 (22.22%)	1 (14.29%)	0 (0.00%)	1 (25.00%)
Leukopenia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Lymphopenia	2 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	1 (20.00%)	0 (0.00%)
Neutropenia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)
Neutrophilia	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Thrombocytopenia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Thrombocytosis	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Cardiac disorders							
Angina pectoris	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)
Bradycardia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)

Sinus tachycardia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	0 (0.00%)
Tachycardia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)
Ear and labyrinth disorders							
Ear pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Endocrine disorders							
Hyperthyroidism	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hypothyroidism	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Eye disorders							
Cataract	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Dry eye	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Eye oedema	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Eye pain	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Eye swelling	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Visual impairment	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Gastrointestinal disorders							
Abdominal distension	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	1 (25.00%)
Abdominal hernia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)
Abdominal pain	2 (33.33%)	1 (33.33%)	0 (0.00%)	1 (11.11%)	2 (28.57%)	1 (20.00%)	1 (25.00%)
Abdominal pain lower	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Abdominal pain upper	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Angular cheilitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Ascites	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	3 (42.86%)	1 (20.00%)	0 (0.00%)
Constipation	2 (33.33%)	2 (66.67%)	0 (0.00%)	3 (33.33%)	2 (28.57%)	1 (20.00%)	1 (25.00%)
Diarrhoea	2 (33.33%)	1 (33.33%)	1 (20.00%)	1 (11.11%)	0 (0.00%)	1 (20.00%)	0 (0.00%)

Dry mouth	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)
Dyspepsia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Dysphagia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Flatulence	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Gastrointestinal sounds abnormal	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Gastrooesophageal reflux disease	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (28.57%)	0 (0.00%)	0 (0.00%)
Nausea	1 (16.67%)	1 (33.33%)	0 (0.00%)	2 (22.22%)	1 (14.29%)	2 (40.00%)	0 (0.00%)
Oesophageal stenosis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Proctalgia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Regurgitation	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Salivary hypersecretion	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)
Small intestinal obstruction	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Stomatitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Tooth loss	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Vomiting	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	1 (14.29%)	0 (0.00%)	1 (25.00%)
General disorders and administration site conditions							
Asthenia	0 (0.00%)	1 (33.33%)	1 (20.00%)	1 (11.11%)	1 (14.29%)	1 (20.00%)	0 (0.00%)
Chest discomfort	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Chest pain	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Chills	1 (16.67%)	0 (0.00%)	1 (20.00%)	2 (22.22%)	0 (0.00%)	2 (40.00%)	2 (50.00%)
Fatigue	1 (16.67%)	2 (66.67%)	1 (20.00%)	0 (0.00%)	1 (14.29%)	4 (80.00%)	1 (25.00%)
Feeling cold	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	1 (20.00%)	0 (0.00%)
Influenza like illness	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Injection site pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Mass	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Nodule	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Non-cardiac chest pain	1 (16.67%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	1 (20.00%)	0 (0.00%)
Oedema peripheral	2 (33.33%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	1 (20.00%)	0 (0.00%)
Pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)
Peripheral swelling	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pyrexia	2 (33.33%)	1 (33.33%)	1 (20.00%)	1 (11.11%)	5 (71.43%)	1 (20.00%)	0 (0.00%)
Hepatobiliary disorders							
Cholangitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	0 (0.00%)
Hyperbilirubinaemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	0 (0.00%)
Liver disorder	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	0 (0.00%)
Immune system disorders							
Contrast media reaction	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Infections and infestations							
Cystitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Herpes zoster	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hordeolum	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	0 (0.00%)
Influenza	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Nasopharyngitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)
Oral candidiasis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	0 (0.00%)
Oral herpes	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pneumonia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Respiratory tract infection	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Upper respiratory tract infection	0 (0.00%)	1 (33.33%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Urinary tract infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Urinary tract infection enterococcal	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Vaginal infection	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Viral upper respiratory tract infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Injury, poisoning and procedural complications							
Eye injury	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Fall	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Infusion related reaction	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	1 (14.29%)	0 (0.00%)	0 (0.00%)
Investigations							
Activated partial thromboplastin time prolonged	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Alanine aminotransferase increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)
Aldolase increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Amylase increased	1 (16.67%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Aspartate aminotransferase increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)
Bilirubin urine	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	0 (0.00%)

Blood alkaline phosphatase increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	0 (0.00%)
Blood creatine phosphokinase increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Blood creatine phosphokinase MB increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Blood creatinine increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Blood lactate dehydrogenase increased	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Blood thyroid stimulating hormone decreased	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Blood thyroid stimulating hormone increased	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Blood urea increased	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Brain natriuretic peptide increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Breath sounds abnormal	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Electrocardiogram QT prolonged	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)
International normalised ratio decreased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Lipase	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Lipase increased	1 (16.67%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Lymphocyte count decreased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	0 (0.00%)
Myoglobin blood increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Myoglobin urine present	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Neutrophil count decreased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Prothrombin time prolonged	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	0 (0.00%)
Red blood cell sedimentation rate increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Thyroxine increased	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Urobilinogen urine increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	0 (0.00%)
Vitamin D decreased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Weight decreased	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)
Weight increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
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%)
Decreased appetite	0 (0.00%)	0 (0.00%)	1 (20.00%)	1 (11.11%)	2 (28.57%)	1 (20.00%)	2 (50.00%)
Dehydration	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hypercalcaemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hypercholesterolaemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hyperglycaemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hyperkalaemia	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hyperphosphataemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)

Hyperuricaemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hypoalbuminaemia	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	0 (0.00%)
Hypocalcaemia	1 (16.67%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hypoglycaemia	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hypokalaemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	1 (25.00%)
Hypomagnesaemia	1 (16.67%)	0 (0.00%)	1 (20.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hyponatraemia	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	0 (0.00%)
Hypophosphataemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (22.22%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Iron deficiency	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Metabolic acidosis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	0 (0.00%)
Musculoskeletal and connective tissue disorders							
Arthralgia	0 (0.00%)	1 (33.33%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	1 (25.00%)
Back pain	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)
Flank pain	1 (16.67%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Joint swelling	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Muscle spasms	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Muscular weakness	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Musculoskeletal chest pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Musculoskeletal discomfort	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Musculoskeletal pain	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Myalgia	3 (50.00%)	0 (0.00%)	0 (0.00%)	2 (22.22%)	1 (14.29%)	1 (20.00%)	1 (25.00%)
Neck mass	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Neck pain	1 (16.67%)	0 (0.00%)	0 (0.00%)	2 (22.22%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pain in extremity	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)

Pain in jaw	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Polyarthritis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)							
Tumour haemorrhage	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Tumour pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Tumour thrombosis	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Nervous system disorders							
Dizziness	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)
Dysgeusia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	0 (0.00%)
Headache	1 (16.67%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)
Hypoaesthesia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)
Neuropathy peripheral	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)
Paraesthesia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	0 (0.00%)
Peripheral sensory neuropathy	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Presyncope	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Restless legs syndrome	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Somnolence	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Syncope	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Taste disorder	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Tremor	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Vocal cord paralysis	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Product issues							
Device failure	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Psychiatric disorders							
Anxiety	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	1 (25.00%)
Apathy	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Confusional state	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Depression	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)
Insomnia	1 (16.67%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	1 (25.00%)
Restlessness	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Renal and urinary disorders							
Dysuria	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Haematuria	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Haemoglobinuria	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Ketonuria	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Polyuria	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Proteinuria	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Renal cyst	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Urine abnormality	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	0 (0.00%)
Reproductive system and breast disorders							
Breast discharge	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Breast pain	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Uterine haemorrhage	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Vaginal discharge	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Vaginal haemorrhage	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Respiratory, thoracic and mediastinal disorders							

Cough	2 (33.33%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	2 (50.00%)
Dysphonia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Dyspnoea	2 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (40.00%)	1 (25.00%)
Dyspnoea exertional	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Epistaxis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)
Haemoptysis	2 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Oropharyngeal pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)
Pleural effusion	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	0 (0.00%)
Pneumothorax	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pulmonary haemorrhage	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Respiratory tract congestion	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Rhinitis allergic	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Rhinorrhoea	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	1 (25.00%)
Sinus congestion	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Sneezing	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Upper respiratory tract inflammation	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	0 (0.00%)
Skin and subcutaneous tissue disorders							
Dermatitis allergic	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Dry skin	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Erythema	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hyperhidrosis	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Night sweats	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pain of skin	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Pruritus	0 (0.00%)	0 (0.00%)	2 (40.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Rash	1 (16.67%)	2 (66.67%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)
Rash maculo-papular	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Rash vesicular	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Skin disorder	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Skin lesion	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Skin toxicity	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Vascular disorders							
Embolism	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Flushing	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hot flush	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hypertension	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hypotension	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)
Peripheral coldness	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	0 (0.00%)

	GWN323 10mg Q3W + PDR001 100mg Q3W N = 6	GWN323 10mg Q3W + PDR001 200mg Q3W N = 4	GWN323 30mg Q3W + PDR001 100mg Q3W N = 4	GWN323 30mg Q3W + PDR001 300mg Q3W N = 5	GWN323 75mg Q3W + PDR001 300mg Q3W N = 5	GWN323 150mg Q3W + PDR001 300mg Q3W N = 17	GWN323 300mg Q3W + PDR001 300mg Q3W N = 7	GWN323 750mg Q3W + PDR001 300mg Q3W N = 5
Arm/Group Description	Combination arm	Combination arm	Combination arm	Combination arm	Combination arm	Combination arm	Combination arm	Combination arm
Total participants affected	6 (100.00%)	3 (75.00%)	4 (100.00%)	5 (100.00%)	5 (100.00%)	17 (100.00%)	6 (85.71%)	5 (100.00%)
Blood and lymphatic system disorders								
Anaemia	1 (16.67%)	1 (25.00%)	0 (0.00%)	2 (40.00%)	0 (0.00%)	2 (11.76%)	3 (42.86%)	0 (0.00%)
Leukopenia	1 (16.67%)	0 (0.00%)	0 (0.00%)	2 (40.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Lymphopenia	1 (16.67%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)	1 (14.29%)	0 (0.00%)
Neutropenia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Neutrophilia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Thrombocytopenia	0 (0.00%)	1 (25.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Thrombocytosis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Cardiac disorders								
Angina pectoris	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Bradycardia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)
Sinus tachycardia	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)
Tachycardia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Ear and labyrinth disorders								
Ear pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)
Endocrine disorders								
Hyperthyroidism	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Hypothyroidism	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)	0 (0.00%)	0 (0.00%)
Eye disorders								
Cataract	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)	0 (0.00%)	0 (0.00%)
Dry eye	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Eye 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%)
Eye 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%)
Eye swelling	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)	0 (0.00%)	0 (0.00%)
Visual impairment	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Gastrointestinal disorders								
Abdominal distension	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)	0 (0.00%)	0 (0.00%)
Abdominal hernia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Abdominal pain	1 (16.67%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	4 (23.53%)	3 (42.86%)	0 (0.00%)
Abdominal pain lower	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Abdominal pain upper	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Angular cheilitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Ascites	1 (16.67%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Constipation	1 (16.67%)	0 (0.00%)	0 (0.00%)	2 (40.00%)	1 (20.00%)	2 (11.76%)	2 (28.57%)	0 (0.00%)
Diarrhoea	3 (50.00%)	0 (0.00%)	1 (25.00%)	1 (20.00%)	0 (0.00%)	4 (23.53%)	2 (28.57%)	0 (0.00%)
Dry mouth	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	1 (5.88%)	0 (0.00%)	1 (20.00%)
Dyspepsia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)	0 (0.00%)	0 (0.00%)
Dysphagia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)	0 (0.00%)	0 (0.00%)
Flatulence	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Gastrointestinal sounds abnormal	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)	0 (0.00%)	0 (0.00%)

Gastrooesophageal reflux disease	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)	0 (0.00%)	0 (0.00%)
Nausea	4 (66.67%)	2 (50.00%)	1 (25.00%)	1 (20.00%)	0 (0.00%)	1 (5.88%)	2 (28.57%)	1 (20.00%)
Oesophageal stenosis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)	0 (0.00%)	0 (0.00%)
Proctalgia	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Regurgitation	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)
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%)
Small intestinal obstruction	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)	0 (0.00%)	0 (0.00%)
Stomatitis	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)
Tooth loss	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Vomiting	2 (33.33%)	1 (25.00%)	1 (25.00%)	1 (20.00%)	1 (20.00%)	1 (5.88%)	2 (28.57%)	0 (0.00%)
General disorders and administration site conditions								
Asthenia	1 (16.67%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Chest discomfort	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)
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%)
Chills	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	1 (20.00%)	4 (23.53%)	1 (14.29%)	1 (20.00%)
Fatigue	3 (50.00%)	0 (0.00%)	2 (50.00%)	2 (40.00%)	3 (60.00%)	4 (23.53%)	1 (14.29%)	0 (0.00%)
Feeling cold	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Influenza like illness	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Injection site pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Mass	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)
Nodule	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Non-cardiac chest pain	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	1 (14.29%)	1 (20.00%)
Oedema peripheral	1 (16.67%)	0 (0.00%)	2 (50.00%)	0 (0.00%)	1 (20.00%)	1 (5.88%)	1 (14.29%)	1 (20.00%)

Pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Peripheral swelling	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)
Pyrexia	1 (16.67%)	1 (25.00%)	1 (25.00%)	0 (0.00%)	1 (20.00%)	5 (29.41%)	1 (14.29%)	1 (20.00%)
Hepatobiliary disorders								
Cholangitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hyperbilirubinaemia	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Liver 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%)
Immune system disorders								
Contrast media reaction	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Infections and infestations								
Cystitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)	0 (0.00%)	0 (0.00%)
Herpes zoster	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hordeolum	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Influenza	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Nasopharyngitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)	0 (0.00%)	0 (0.00%)
Oral candidiasis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)	0 (0.00%)	0 (0.00%)
Oral herpes	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pneumonia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)	0 (0.00%)	0 (0.00%)
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%)
Upper respiratory tract infection	1 (16.67%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Urinary tract infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	3 (17.65%)	0 (0.00%)	1 (20.00%)
Urinary tract infection enterococcal	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)

Vaginal 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%)
Viral upper 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%)
Injury, poisoning and procedural complications								
Eye injury	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)	0 (0.00%)	0 (0.00%)
Fall	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Infusion related reaction	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	1 (20.00%)	1 (5.88%)	0 (0.00%)	0 (0.00%)
Investigations								
Activated partial thromboplastin time prolonged	1 (16.67%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Alanine aminotransferase increased	0 (0.00%)	0 (0.00%)	1 (25.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Aldolase increased	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Amylase increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)	1 (14.29%)	0 (0.00%)
Aspartate aminotransferase increased	2 (33.33%)	0 (0.00%)	2 (50.00%)	1 (20.00%)	0 (0.00%)	1 (5.88%)	0 (0.00%)	0 (0.00%)
Bilirubin urine	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Blood alkaline phosphatase increased	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Blood creatine phosphokinase increased	0 (0.00%)	1 (25.00%)	1 (25.00%)	1 (20.00%)	0 (0.00%)	1 (5.88%)	1 (14.29%)	0 (0.00%)
Blood creatine phosphokinase MB increased	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Blood creatinine increased	1 (16.67%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	1 (20.00%)	2 (11.76%)	1 (14.29%)	1 (20.00%)
Blood lactate dehydrogenase increased	1 (16.67%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)	0 (0.00%)	0 (0.00%)
Blood thyroid stimulating hormone decreased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Blood thyroid stimulating hormone increased	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)
Blood urea increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	1 (5.88%)	0 (0.00%)	0 (0.00%)
Brain natriuretic peptide increased	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Breath sounds abnormal	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
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%)
International normalised ratio decreased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)
Lipase	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)
Lipase increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	3 (17.65%)	0 (0.00%)	0 (0.00%)
Lymphocyte count decreased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Myoglobin blood increased	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Myoglobin urine present	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Neutrophil count decreased	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Prothrombin time prolonged	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Red blood cell sedimentation rate increased	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Thyroxine 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%)
Urobilinogen urine 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%)
Vitamin D decreased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)	0 (0.00%)	0 (0.00%)
Weight decreased	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)
Weight increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)	0 (0.00%)	0 (0.00%)
Metabolism and nutrition disorders								
Cachexia	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Decreased appetite	3 (50.00%)	1 (25.00%)	3 (75.00%)	2 (40.00%)	1 (20.00%)	2 (11.76%)	1 (14.29%)	1 (20.00%)
Dehydration	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	1 (20.00%)
Hypercalcaemia	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hypercholesterolaemia	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hyperglycaemia	1 (16.67%)	1 (25.00%)	1 (25.00%)	1 (20.00%)	1 (20.00%)	1 (5.88%)	0 (0.00%)	0 (0.00%)
Hyperkalaemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	1 (5.88%)	0 (0.00%)	0 (0.00%)
Hyperphosphataemia	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hyperuricaemia	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)
Hypoalbuminaemia	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)	1 (14.29%)	0 (0.00%)
Hypocalcaemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)
Hypoglycaemia	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)	0 (0.00%)	0 (0.00%)
Hypokalaemia	1 (16.67%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)	0 (0.00%)	0 (0.00%)
Hypomagnesaemia	1 (16.67%)	2 (50.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	1 (5.88%)	0 (0.00%)	0 (0.00%)

Hyponatraemia	1 (16.67%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)
Hypophosphataemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)	1 (14.29%)	0 (0.00%)
Iron deficiency	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)
Metabolic acidosis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Musculoskeletal and connective tissue disorders								
Arthralgia	1 (16.67%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	3 (17.65%)	0 (0.00%)	0 (0.00%)
Back pain	2 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	3 (17.65%)	2 (28.57%)	1 (20.00%)
Flank pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)
Joint swelling	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Muscle spasms	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (11.76%)	0 (0.00%)	0 (0.00%)
Muscular weakness	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	1 (14.29%)	1 (20.00%)
Musculoskeletal chest pain	1 (16.67%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Musculoskeletal discomfort	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)	0 (0.00%)	0 (0.00%)
Musculoskeletal pain	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Myalgia	2 (33.33%)	1 (25.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)	0 (0.00%)	0 (0.00%)
Neck mass	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)	0 (0.00%)	0 (0.00%)
Neck 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%)
Pain in extremity	1 (16.67%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)
Pain in jaw	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Polyarthritis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)	0 (0.00%)	0 (0.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)								
Tumour haemorrhage	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)	0 (0.00%)	0 (0.00%)
Tumour pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)	1 (14.29%)	0 (0.00%)

Tumour thrombosis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Nervous system disorders								
Dizziness	1 (16.67%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	1 (20.00%)
Dysgeusia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Headache	1 (16.67%)	0 (0.00%)	0 (0.00%)	2 (40.00%)	1 (20.00%)	3 (17.65%)	0 (0.00%)	1 (20.00%)
Hypoaesthesia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Neuropathy peripheral	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Paraesthesia	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)	0 (0.00%)	0 (0.00%)
Peripheral sensory neuropathy	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Presyncope	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Restless legs syndrome	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)	0 (0.00%)	0 (0.00%)
Somnolence	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)	0 (0.00%)	0 (0.00%)
Syncope	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Taste disorder	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Tremor	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)	0 (0.00%)	0 (0.00%)
Vocal cord paralysis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Product issues								
Device failure	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Psychiatric disorders								
Anxiety	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Apathy	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Confusional state	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Depression	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)	0 (0.00%)	0 (0.00%)

Insomnia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (11.76%)	0 (0.00%)	1 (20.00%)
Restlessness	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Renal and urinary disorders								
Dysuria	2 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Haematuria	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)
Haemoglobinuria	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Ketonuria	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Polyuria	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Proteinuria	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Renal cyst	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Urine abnormality	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Reproductive system and breast disorders								
Breast discharge	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Breast 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%)
Uterine haemorrhage	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)	0 (0.00%)	0 (0.00%)
Vaginal discharge	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)	0 (0.00%)	0 (0.00%)
Vaginal haemorrhage	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)	0 (0.00%)	0 (0.00%)
Respiratory, thoracic and mediastinal disorders								
Cough	3 (50.00%)	0 (0.00%)	2 (50.00%)	1 (20.00%)	0 (0.00%)	4 (23.53%)	0 (0.00%)	0 (0.00%)
Dysphonia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Dyspnoea	1 (16.67%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)	0 (0.00%)	1 (20.00%)
Dyspnoea exertional	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
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%)
Haemoptysis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)

Oropharyngeal pain	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
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%)
Pneumothorax	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pulmonary haemorrhage	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Respiratory tract congestion	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Rhinitis allergic	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (11.76%)	0 (0.00%)	0 (0.00%)
Rhinorrhoea	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)	0 (0.00%)	0 (0.00%)
Sinus congestion	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Sneezing	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Upper respiratory tract inflammation	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Skin and subcutaneous tissue disorders								
Dermatitis allergic	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Dry skin	0 (0.00%)	0 (0.00%)	1 (25.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Erythema	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)	0 (0.00%)	0 (0.00%)
Hyperhidrosis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Night sweats	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)	0 (0.00%)	0 (0.00%)
Pain of skin	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)
Pruritus	0 (0.00%)	0 (0.00%)	1 (25.00%)	2 (40.00%)	0 (0.00%)	5 (29.41%)	0 (0.00%)	0 (0.00%)
Rash	2 (33.33%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	3 (17.65%)	2 (28.57%)	1 (20.00%)
Rash maculo-papular	0 (0.00%)	0 (0.00%)	1 (25.00%)	2 (40.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Rash vesicular	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Skin disorder	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)	0 (0.00%)	0 (0.00%)
Skin lesion	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Skin toxicity	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)	0 (0.00%)	0 (0.00%)
Vascular disorders								
Embolism	0 (0.00%)	1 (25.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Flushing	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hot flush	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hypertension	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	1 (20.00%)
Hypotension	1 (16.67%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)
Peripheral coldness	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Conclusion:

- The study was terminated early after review of the available data showed minimal antitumor activity. The maximum administered dose (MAD) was declared and therefore, dose was not escalated further. Due to minimal anti-tumor activity observed, the dose expansion part was not initiated.
- The termination of study GWN323X2101 was not a consequence of any safety concern and has no impact on any other clinical trials involving GWN323 or PDR001 (spartalizumab).
- The treatment with GWN323 both as single agent and in combination with PDR001was well tolerated and no significant safety findings were observed.
- Pharmacokinetics (PK) of GWN323 follows typical monoclonal antibody behavior with dose dependent increase in PK exposure. No drug-drug interaction was observed between GWN323 and PDR001.
- In both single agent and combination arms there was modest evidence of a treatment-induced ADA response.

- The median T-cell ratio in the single agent GWN323 arms at baseline, Cycle 2 Day 1 and Cycle 4 Day 1 was 4.1, 3.9 and 45.7, respectively, and in the combination GWN323 and PDR001 arms median T-cell ratio was 6.2, 5.2 and 6.0, respectively.

Date of Clinical Trial Report

27-Jan-2021