Clinical trial results:
A Two-Cohort Randomized Phase II, Double-Blind, Parallel Group Study in Patients with Active Rheumatoid Arthritis Evaluating the Efficacy and Safety of GDC-0853 Compared with Placebo and Adalimumab in Patients with an Inadequate Response to Previous Methotrexate Therapy (Cohort 1) and Compared with Placebo in Patients with an Inadequate Response or Intolerance to Previous TNF Therapy (Cohort 2).

Summary

EudraCT number	2016-000335-40
Trial protocol	BG
Global end of trial date	02 July 2018

Results information

Result version number	v1 (current)
This version publication date	18 July 2019
First version publication date	18 July 2019

Trial information

Trial identification

Sponsor protocol code	GA29350

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02833350
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Hoffmann-La Roche AG
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, CH-4070
Public contact	Hoffmann-La Roche AG, Hoffmann-La Roche AG, 41 616878333, global.trial_information@roche.com
Scientific contact	Medical Communications, Hoffmann-La Roche AG, 41 616878333, globa.trial_information@roche.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	02 July 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	02 July 2018
Global end of trial reached?	Yes
Global end of trial date	02 July 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy and safety of GDC-0853 in patients with moderate to severe active RA and an inadequate response to previous MTX therapy (Cohort 1) or MTX and TNF therapy who may have also had exposure to no more than one non-TNF inhibitor biologic (Cohort 2).

Protection of trial subjects:

All study subjects were required to read and sign an Informed Consent Form.

Background therapy:

Patients with moderate to severe active (RA) and an inadequate response to previous methotrexate (MTX) therapy (Cohort 1) or inadequate response or intolerance to one or two TNF inhibitors and MTX therapy, and who may have also had exposure to no more than one non-TNF inhibitor biologic (Cohort 2).

Evidence for comparator: -

Actual start date of recruitment	09 September 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 63
Country: Number of subjects enrolled	Brazil: 56
Country: Number of subjects enrolled	Bulgaria: 40
Country: Number of subjects enrolled	Colombia: 31
Country: Number of subjects enrolled	Mexico: 46
Country: Number of subjects enrolled	Russian Federation: 91
Country: Number of subjects enrolled	Serbia: 37
Country: Number of subjects enrolled	Ukraine: 154
Country: Number of subjects enrolled	United States: 27
Country: Number of subjects enrolled	Poland: 33
Worldwide total number of subjects	578
EEA total number of subjects	73

Notes:

Subjects enrolled per age group

In utero	0

Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	506
From 65 to 84 years	72
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

578 participants were enrolled in the study and 578 were dosed. One (1) subject in Cohort 2 in the Placebo arm was incorrectly dosed with the High Dose. The ITT data set included participants according to their randomization while SAF data set included participants according to the treatment administered.

Pre-assignment

Screening details:

Participants with moderate to severe active RA and an inadequate response to previous MTX therapy (Cohort 1) or inadequate response or intolerance to one or two TNF inhibitors and MTX therapy, and who may have also had exposure to no more than one non-TNF inhibitor biologic (Cohort 2).

Period 1

Period 1 title	Randomized
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1: GDC-0853 Low Dose + Adalimumab Placebo

Arm description:

Participants of Cohort 1 received GDC-0853 low dose, orally once daily along with placebo matched to adalimumab, subcutaneously Q2W starting on Day 1 for 12 weeks. Participants remained on a stable background therapy of MTX 15-25 mg/week (oral or parenteral; for participants entering the trial on MTX doses 15 mg/week, doses as low as 7.5 mg/week were allowed only if there was clear documentation in the medical record that higher doses were not tolerated or that the dose of MTX is the highest acceptable dose based on local clinical practice guidelines) and folic acid of at least 5 mg total dose weekly (or equivalent) as per investigator's discretion.

Arm type	Experimental
Investigational medicinal product name	GDC-0853
Investigational medicinal product code	
Other name	Fenebrutinib
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

50 mg

Investigational medicinal product name	Adalimumab Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

N/A

Arm title	Cohort 1: GDC-0853 Mid Dose + Adalimumab Placebo

Arm description:

Participants of Cohort 1 received GDC-0853 mid dose, orally twice daily along with placebo matched to adalimumab, subcutaneously Q2W starting on Day 1 for 12 weeks. Participants remained on a stable background therapy of MTX 15-25 mg/week (oral or parenteral; for participants entering the trial on MTX doses 15 mg/week, doses as low as 7.5 mg/week were allowed only if there was clear documentation in the medical record that higher doses were not tolerated or that the dose of MTX was the highest acceptable dose based on local clinical practice guidelines) and folic acid of at least 5 mg total dose weekly (or equivalent) as per investigator's discretion.

Arm type	Experimental
Investigational medicinal product name	Adalimumab Placeb
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

N/A

Investigational medicinal product name	GDC-0853
Investigational medicinal product code	
Other name	Fenebrutinib
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

150 MG

Arm title	Cohort 1: GDC-0853 High Dose + Adalimumab Placebo

Arm description:

Participants of Cohort 1 received GDC-0853 high dose, orally once daily along with placebo matched to adalimumab, subcutaneously every 2 weeks (Q2W) starting on Day 1 for 12 weeks. Participants remained on a stable background therapy of MTX 15-25 milligrams per week (mg/week) (oral or parenteral; for participants entering the trial on MTX doses 15 mg/week, doses as low as 7.5 mg/week were allowed only if there was clear documentation in the medical record that higher doses were not tolerated or that the dose of MTX was the highest acceptable dose based on local clinical practice guidelines) and folic acid of at least 5 mg total dose weekly (or equivalent) as per investigator's discretion.

Arm type	Experimental
Investigational medicinal product name	Adalimumab Placeb
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

N/A

Investigational medicinal product name	GDC-0853
Investigational medicinal product code	
Other name	Fenebrutinib
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

200 mg

Arm title	Cohort 1: GDC-0853 Placebo + Adalimumab Placebo

Arm description:

Participants of Cohort 1 received placebo matched to GDC-0853, orally once daily along with placebo matched to adalimumab, subcutaneously Q2W starting on Day 1 for 12 weeks. Participants remained on a stable background therapy of MTX 15-25 mg/week (oral or parenteral; for participants entering the trial on MTX doses 15 mg/week, doses as low as 7.5 mg/week were allowed only if there was clear documentation in the medical record that higher doses were not tolerated or that the dose of MTX is the highest acceptable dose based on local clinical practice guidelines) and folic acid of at least 5 mg total dose weekly (or equivalent) as per investigator's discretion.

Arm type	Placebo

Investigational medicinal product name	GDC-0853 Placebo
Investigational medicinal product code	
Other name	Fenebrutinib Placebo
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

N/A

Investigational medicinal product name	Adalimumab Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

N/A

Arm title	Cohort 1: GDC-0853 Placebo + Adalimumab

Arm description:

Participants of Cohort 1 received placebo matched to GDC-0853, orally once daily along with adalimumab, subcutaneously Q2W starting on Day 1 for 12 weeks. Participants remained on a stable background therapy of MTX 15-25 mg/week (oral or parenteral; for participants entering the trial on MTX doses 15 mg/week, doses as low as 7.5 mg/week were allowed only if there was clear documentation in the medical record that higher doses were not tolerated or that the dose of MTX is the highest acceptable dose based on local clinical practice guidelines) and folic acid of at least 5 mg total dose weekly (or equivalent) as per investigator's discretion.

Arm type	Active comparator
Investigational medicinal product name	Adalimumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

40 mg

Investigational medicinal product name	GDC-0853 Placebo
Investigational medicinal product code	
Other name	GDC-0853 Placebo
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

N/A

Arm title	Cohort 2: GDC-0853 High Dose

Arm description:

Participants of Cohort 2 received GDC-0853 high dose, orally twice daily for 12 weeks. Participants remained on a stable background therapy of MTX 15-25 mg/week (oral or parenteral; for participants entering the trial on MTX doses 15 mg/week, doses as low as 7.5 mg/week were allowed only if there was clear documentation in the medical record that higher doses were not tolerated or that the dose of MTX is the highest acceptable dose based on local clinical practice guidelines) and folic acid of at least 5 mg total dose weekly (or equivalent) as per investigator's discretion.

Arm type	Experimental
Investigational medicinal product name	GDC-0853
Investigational medicinal product code	
Other name	Fenebrutinib
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

200 mg

Arm title	Cohort 2: GDC-0853 Placebo

Arm description:

Participants of Cohort 2 received placebo matched to GDC-0853, orally twice daily for 12 weeks. Participants remained on a stable background therapy of MTX 15-25 mg/week (oral or parenteral; for participants entering the trial on MTX doses 15 mg/week, doses as low as 7.5 mg/week were allowed only if there was clear documentation in the medical record that higher doses were not tolerated or that the dose of MTX is the highest acceptable dose based on local clinical practice guidelines) and folic acid of at least 5 mg total dose weekly (or equivalent) as per investigator's discretion.

Arm type	Placebo
Investigational medicinal product name	GDC-0853 Placebo
Investigational medicinal product code	
Other name	Fenebrutinib Placebo
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

N/A

Number of subjects in period 1	Cohort 1: GDC-0853 Low Dose + Adalimumab Placebo	Cohort 1: GDC-0853 Mid Dose + Adalimumab Placebo	Cohort 1: GDC-0853 High Dose + Adalimumab Placebo
Started	40	109	110
Completed	40	109	110

Number of subjects in period 1	Cohort 1: GDC-0853 Placebo + Adalimumab Placebo	Cohort 1: GDC-0853 Placebo + Adalimumab	Cohort 2: GDC-0853 High Dose
Started	110	111	48
Completed	110	111	48

Number of subjects in period 1	Cohort 2: GDC-0853 Placebo
Started	50
Completed	50

Period 2

Period 2 title	Treated
Is this the baseline period?	Yes[1]
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes

Arm title	Cohort 1: GDC-0853 Low Dose + Adalimumab Placebo

Arm description:

Participants of Cohort 1 will receive GDC-0853 low dose, orally once daily along with placebo matched to adalimumab, subcutaneously Q2W starting on Day 1 for 12 weeks. Participants will remain on a stable background therapy of MTX 15-25 mg/week (oral or parenteral; for participants entering the trial on MTX doses 15 mg/week, doses as low as 7.5 mg/week are allowed only if there is clear documentation in the medical record that higher doses were not tolerated or that the dose of MTX is the highest acceptable dose based on local clinical practice guidelines) and folic acid of at least 5 mg total dose weekly (or equivalent) as per investigator's discretion.

Arm type	Experimental
Investigational medicinal product name	Adalimumab Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

N/A

Investigational medicinal product name	GDC-0853
Investigational medicinal product code	
Other name	Fenebrutinib
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

50 mg

Arm title	Cohort 1: GDC-0853 Mid Dose + Adalimumab Placebo

Arm description:

Participants of Cohort 1 will receive GDC-0853 mid dose, orally twice daily along with placebo matched to adalimumab, subcutaneously Q2W starting on Day 1 for 12 weeks. Participants will remain on a stable background therapy of MTX 15-25 mg/week (oral or parenteral; for participants entering the trial on MTX doses 15 mg/week, doses as low as 7.5 mg/week are allowed only if there is clear documentation in the medical record that higher doses were not tolerated or that the dose of MTX is the highest acceptable dose based on local clinical practice guidelines) and folic acid of at least 5 mg total dose weekly (or equivalent) as per investigator's discretion.

Arm type	Experimental
Investigational medicinal product name	Adalimumab Placeb
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

N/A

Investigational medicinal product name	GDC-0853
Investigational medicinal product code	
Other name	Fenebrutinib
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

150 MG

Arm title	Cohort 1: GDC-0853 High Dose + Adalimumab Placebo

Arm description:

Participants of Cohort 1 will receive GDC-0853 high dose, orally once daily along with placebo matched to adalimumab, subcutaneously every 2 weeks (Q2W) starting on Day 1 for 12 weeks. Participants will remain on a stable background therapy of MTX 15-25 milligrams per week (mg/week) (oral or parenteral; for participants entering the trial on MTX doses 15 mg/week, doses as low as 7.5 mg/week are allowed only if there is clear documentation in the medical record that higher doses were not

tolerated or that the dose of MTX is the highest acceptable dose based on local clinical practice guidelines) and folic acid of at least 5 mg total dose weekly (or equivalent) as per investigator's discretion.

Arm type	Experimental
Investigational medicinal product name	Adalimumab Placeb
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

N/A

Investigational medicinal product name	GDC-0853
Investigational medicinal product code	
Other name	Fenebrutinib
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

200 mg

Arm title	Cohort 1: GDC-0853 Placebo + Adalimumab Placebo

Arm description:

Participants of Cohort 1 will receive placebo matched to GDC-0853, orally once daily along with placebo matched to adalimumab, subcutaneously Q2W starting on Day 1 for 12 weeks. Participants will remain on a stable background therapy of MTX 15-25 mg/week (oral or parenteral; for participants entering the trial on MTX doses 15 mg/week, doses as low as 7.5 mg/week are allowed only if there is clear documentation in the medical record that higher doses were not tolerated or that the dose of MTX is the highest acceptable dose based on local clinical practice guidelines) and folic acid of at least 5 mg total dose weekly (or equivalent) as per investigator's discretion.

Arm type	Placebo
Investigational medicinal product name	Adalimumab Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

N/A

Investigational medicinal product name	GDC-0853 Placebo
Investigational medicinal product code	
Other name	Fenebrutinib Placebo
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

N/A

Arm title	Cohort 1: GDC-0853 Placebo + Adalimumab

Arm description:

Participants of Cohort 1 will receive placebo matched to GDC-0853, orally once daily along with adalimumab, subcutaneously Q2W starting on Day 1 for 12 weeks. Participants will remain on a stable background therapy of MTX 15-25 mg/week (oral or parenteral; for participants entering the trial on MTX doses 15 mg/week, doses as low as 7.5 mg/week are allowed only if there is clear documentation in the medical record that higher doses were not tolerated or that the dose of MTX is the highest acceptable dose based on local clinical practice guidelines) and folic acid of at least 5 mg total dose weekly (or equivalent) as per investigator's discretion.

Arm type	Active comparator

Investigational medicinal product name	GDC-0853 Placebo
Investigational medicinal product code	
Other name	GDC-0853 Placebo
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

N/A

Investigational medicinal product name	Adalimumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

40 mg

Arm title	Cohort 2: GDC-0853 High Dose

Arm description:

Participants of Cohort 2 will receive GDC-0853 high dose, orally twice daily for 12 weeks. Participants will remain on a stable background therapy of MTX 15-25 mg/week (oral or parenteral; for participants entering the trial on MTX doses 15 mg/week, doses as low as 7.5 mg/week are allowed only if there is clear documentation in the medical record that higher doses were not tolerated or that the dose of MTX is the highest acceptable dose based on local clinical practice guidelines) and folic acid of at least 5 mg total dose weekly (or equivalent) as per investigator's discretion.

Arm type	Experimental
Investigational medicinal product name	GDC-0853
Investigational medicinal product code	
Other name	Fenebrutinib
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

200 mg

Arm title	Cohort 2: GDC-0853 Placebo

Arm description:

Participants of Cohort 2 will receive placebo matched to GDC-0853, orally twice daily for 12 weeks. Participants will remain on a stable background therapy of MTX 15-25 mg/week (oral or parenteral; for participants entering the trial on MTX doses 15 mg/week, doses as low as 7.5 mg/week are allowed only if there is clear documentation in the medical record that higher doses were not tolerated or that the dose of MTX is the highest acceptable dose based on local clinical practice guidelines) and folic acid of at least 5 mg total dose weekly (or equivalent) as per investigator's discretion.

Arm type	Placebo
Investigational medicinal product name	GDC-0853 Placebo
Investigational medicinal product code	
Other name	Fenebrutinib Placebo
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

N/A

Notes:

[1] - Period 1 is not the baseline period. It is expected that period 1 will be the baseline period.

Justification: This endpoint was specific for Cohort 1 only.

Number of subjects in period 2	Cohort 1: GDC-0853 Low Dose + Adalimumab Placebo	Cohort 1: GDC-0853 Mid Dose + Adalimumab Placebo	Cohort 1: GDC-0853 High Dose + Adalimumab Placebo
Started	40	109	110
Completed	37	100	102
Not completed	3	9	8
Adverse event, serious fatal	-	-	1
Consent withdrawn by subject	3	3	2
Adverse event, non-fatal	-	3	4
Lost to follow-up	-	1	-
Lack of efficacy	-	2	1

Number of subjects in period 2	Cohort 1: GDC-0853 Placebo + Adalimumab Placebo	Cohort 1: GDC-0853 Placebo + Adalimumab	Cohort 2: GDC-0853 High Dose
Started	110	111	49
Completed	102	108	48
Not completed	8	3	1
Adverse event, serious fatal	-	-	-
Consent withdrawn by subject	-	2	-
Adverse event, non-fatal	4	1	-
Lost to follow-up	-	-	-
Lack of efficacy	4	-	1

Number of subjects in period 2	Cohort 2: GDC-0853 Placebo
Started	49
Completed	44
Not completed	5
Adverse event, serious fatal	-
Consent withdrawn by subject	2
Adverse event, non-fatal	1
Lost to follow-up	1
Lack of efficacy	1

Baseline characteristics

Reporting groups

Reporting group title	Cohort 1: GDC-0853 Low Dose + Adalimumab Placebo

Reporting group description:

Participants of Cohort 1 will receive GDC-0853 low dose, orally once daily along with placebo matched to adalimumab, subcutaneously Q2W starting on Day 1 for 12 weeks. Participants will remain on a stable background therapy of MTX 15-25 mg/week (oral or parenteral; for participants entering the trial on MTX doses 15 mg/week, doses as low as 7.5 mg/week are allowed only if there is clear documentation in the medical record that higher doses were not tolerated or that the dose of MTX is the highest acceptable dose based on local clinical practice guidelines) and folic acid of at least 5 mg total dose weekly (or equivalent) as per investigator's discretion.

Reporting group title	Cohort 1: GDC-0853 Mid Dose + Adalimumab Placebo

Reporting group description:

Participants of Cohort 1 will receive GDC-0853 mid dose, orally twice daily along with placebo matched to adalimumab, subcutaneously Q2W starting on Day 1 for 12 weeks. Participants will remain on a stable background therapy of MTX 15-25 mg/week (oral or parenteral; for participants entering the trial on MTX doses 15 mg/week, doses as low as 7.5 mg/week are allowed only if there is clear documentation in the medical record that higher doses were not tolerated or that the dose of MTX is the highest acceptable dose based on local clinical practice guidelines) and folic acid of at least 5 mg total dose weekly (or equivalent) as per investigator's discretion.

Reporting group title	Cohort 1: GDC-0853 High Dose + Adalimumab Placebo

Reporting group description:

Participants of Cohort 1 will receive GDC-0853 high dose, orally once daily along with placebo matched to adalimumab, subcutaneously every 2 weeks (Q2W) starting on Day 1 for 12 weeks. Participants will remain on a stable background therapy of MTX 15-25 milligrams per week (mg/week) (oral or parenteral; for participants entering the trial on MTX doses 15 mg/week, doses as low as 7.5 mg/week are allowed only if there is clear documentation in the medical record that higher doses were not tolerated or that the dose of MTX is the highest acceptable dose based on local clinical practice guidelines) and folic acid of at least 5 mg total dose weekly (or equivalent) as per investigator's discretion.

Reporting group title	Cohort 1: GDC-0853 Placebo + Adalimumab Placebo

Reporting group description:

Participants of Cohort 1 will receive placebo matched to GDC-0853, orally once daily along with placebo matched to adalimumab, subcutaneously Q2W starting on Day 1 for 12 weeks. Participants will remain on a stable background therapy of MTX 15-25 mg/week (oral or parenteral; for participants entering the trial on MTX doses 15 mg/week, doses as low as 7.5 mg/week are allowed only if there is clear documentation in the medical record that higher doses were not tolerated or that the dose of MTX is the highest acceptable dose based on local clinical practice guidelines) and folic acid of at least 5 mg total dose weekly (or equivalent) as per investigator's discretion.

Reporting group title	Cohort 1: GDC-0853 Placebo + Adalimumab

Reporting group description:

Participants of Cohort 1 will receive placebo matched to GDC-0853, orally once daily along with adalimumab, subcutaneously Q2W starting on Day 1 for 12 weeks. Participants will remain on a stable background therapy of MTX 15-25 mg/week (oral or parenteral; for participants entering the trial on MTX doses 15 mg/week, doses as low as 7.5 mg/week are allowed only if there is clear documentation in the medical record that higher doses were not tolerated or that the dose of MTX is the highest acceptable dose based on local clinical practice guidelines) and folic acid of at least 5 mg total dose weekly (or equivalent) as per investigator's discretion.

Reporting group title	Cohort 2: GDC-0853 High Dose

Reporting group description:

Participants of Cohort 2 will receive GDC-0853 high dose, orally twice daily for 12 weeks. Participants will remain on a stable background therapy of MTX 15-25 mg/week (oral or parenteral; for participants entering the trial on MTX doses 15 mg/week, doses as low as 7.5 mg/week are allowed only if there is clear documentation in the medical record that higher doses were not tolerated or that the dose of MTX is the highest acceptable dose based on local clinical practice guidelines) and folic acid of at least 5 mg total dose weekly (or equivalent) as per investigator's discretion.

Reporting group title	Cohort 2: GDC-0853 Placebo

Reporting group description:

Participants of Cohort 2 will receive placebo matched to GDC-0853, orally twice daily for 12 weeks. Participants will remain on a stable background therapy of MTX 15-25 mg/week (oral or parenteral; for

participants entering the trial on MTX doses 15 mg/week, doses as low as 7.5 mg/week are allowed only if there is clear documentation in the medical record that higher doses were not tolerated or that the dose of MTX is the highest acceptable dose based on local clinical practice guidelines) and folic acid of at least 5 mg total dose weekly (or equivalent) as per investigator's discretion.

Reporting group values	Cohort 1: GDC-0853 Low Dose + Adalimumab Placebo	Cohort 1: GDC-0853 Mid Dose + Adalimumab Placebo	Cohort 1: GDC-0853 High Dose + Adalimumab Placebo
Number of subjects	40	109	110
Age Categorical Units: Subjects			
<=18 years	0	0	0
Between 18 and 65 years	35	95	99
>=65 years	5	14	11
Age Continuous Units: Years			
arithmetic mean	52.3	50.4	49.9
standard deviation	± 12.0	± 11.0	± 12.4
Sex: Female, Male Units: Subjects			
Female	35	92	85
Male	5	17	25
Race/Ethnicity, Customized			
Race			
Units: Subjects			
American Indian or Alaska native	0	8	12
Asian	1	0	0
Black of African American	0	1	2
White	36	96	96
Multiple	3	2	0
Unknown	0	2	0
Race/Ethnicity, Customized			
Ethnicity			
Units: Subjects			
Hispanic or Latino	8	38	40
Not Hispanic or Latino	31	68	69
Not Stated	0	1	1
Unknown	1	2	0

Reporting group values	Cohort 1: GDC-0853 Placebo + Adalimumab Placebo	Cohort 1: GDC-0853 Placebo + Adalimumab	Cohort 2: GDC-0853 High Dose
Number of subjects	110	111	49
Age Categorical Units: Subjects			
<=18 years	0	0	0
Between 18 and 65 years	98	98	41
>=65 years	12	13	8
Age Continuous Units: Years			
arithmetic mean	50.2	49.9	51.3
standard deviation	± 11.6	± 12.4	± 13.2

Sex: Female, Male Units: Subjects			
Female	90	87	37
Male	20	24	12
Race/Ethnicity, Customized			
Race			
Units: Subjects			
American Indian or Alaska native	11	9	6
Asian	0	0	0
Black of African American	3	1	1
White	95	99	42
Multiple	1	1	0
Unknown	0	1	0
Race/Ethnicity, Customized			
Ethnicity			
Units: Subjects			
Hispanic or Latino	38	39	17
Not Hispanic or Latino	72	70	32
Not Stated	0	0	0
Unknown	0	2	0

Reporting group values	Cohort 2: GDC-0853 Placebo	Total	
Number of subjects	49	578	
Age Categorical Units: Subjects			
<=18 years	0	0	
Between 18 and 65 years	40	506	
>=65 years	9	72	
Age Continuous Units: Years			
arithmetic mean	54.6		
standard deviation	± 11.5	-	
Sex: Female, Male Units: Subjects			
Female	37	463	
Male	12	115	
Race/Ethnicity, Customized			
Race			
Units: Subjects			
American Indian or Alaska native	5	51	
Asian	0	1	
Black of African American	2	10	
White	42	506	
Multiple	0	7	
Unknown	0	3	
Race/Ethnicity, Customized			
Ethnicity			
Units: Subjects			
Hispanic or Latino	15	195	
Not Hispanic or Latino	33	375	
Not Stated	1	3	

Unknown	0	5	

End points

End points reporting groups

Reporting group title	Cohort 1: GDC-0853 Low Dose + Adalimumab Placebo

Reporting group description:

Participants of Cohort 1 received GDC-0853 low dose, orally once daily along with placebo matched to adalimumab, subcutaneously Q2W starting on Day 1 for 12 weeks. Participants remained on a stable background therapy of MTX 15-25 mg/week (oral or parenteral; for participants entering the trial on MTX doses 15 mg/week, doses as low as 7.5 mg/week were allowed only if there was clear documentation in the medical record that higher doses were not tolerated or that the dose of MTX is the highest acceptable dose based on local clinical practice guidelines) and folic acid of at least 5 mg total dose weekly (or equivalent) as per investigator's discretion.

Reporting group title	Cohort 1: GDC-0853 Mid Dose + Adalimumab Placebo

Reporting group description:

Participants of Cohort 1 received GDC-0853 mid dose, orally twice daily along with placebo matched to adalimumab, subcutaneously Q2W starting on Day 1 for 12 weeks. Participants remained on a stable background therapy of MTX 15-25 mg/week (oral or parenteral; for participants entering the trial on MTX doses 15 mg/week, doses as low as 7.5 mg/week were allowed only if there was clear documentation in the medical record that higher doses were not tolerated or that the dose of MTX was the highest acceptable dose based on local clinical practice guidelines) and folic acid of at least 5 mg total dose weekly (or equivalent) as per investigator's discretion.

Reporting group title	Cohort 1: GDC-0853 High Dose + Adalimumab Placebo

Reporting group description:

Participants of Cohort 1 received GDC-0853 high dose, orally once daily along with placebo matched to adalimumab, subcutaneously every 2 weeks (Q2W) starting on Day 1 for 12 weeks. Participants remained on a stable background therapy of MTX 15-25 milligrams per week (mg/week) (oral or parenteral; for participants entering the trial on MTX doses 15 mg/week, doses as low as 7.5 mg/week were allowed only if there was clear documentation in the medical record that higher doses were not tolerated or that the dose of MTX was the highest acceptable dose based on local clinical practice guidelines) and folic acid of at least 5 mg total dose weekly (or equivalent) as per investigator's discretion.

Reporting group title	Cohort 1: GDC-0853 Placebo + Adalimumab Placebo

Reporting group description:

Participants of Cohort 1 received placebo matched to GDC-0853, orally once daily along with placebo matched to adalimumab, subcutaneously Q2W starting on Day 1 for 12 weeks. Participants remained on a stable background therapy of MTX 15-25 mg/week (oral or parenteral; for participants entering the trial on MTX doses 15 mg/week, doses as low as 7.5 mg/week were allowed only if there was clear documentation in the medical record that higher doses were not tolerated or that the dose of MTX is the highest acceptable dose based on local clinical practice guidelines) and folic acid of at least 5 mg total dose weekly (or equivalent) as per investigator's discretion.

Reporting group title	Cohort 1: GDC-0853 Placebo + Adalimumab

Reporting group description:

Participants of Cohort 1 received placebo matched to GDC-0853, orally once daily along with adalimumab, subcutaneously Q2W starting on Day 1 for 12 weeks. Participants remained on a stable background therapy of MTX 15-25 mg/week (oral or parenteral; for participants entering the trial on MTX doses 15 mg/week, doses as low as 7.5 mg/week were allowed only if there was clear documentation in the medical record that higher doses were not tolerated or that the dose of MTX is the highest acceptable dose based on local clinical practice guidelines) and folic acid of at least 5 mg total dose weekly (or equivalent) as per investigator's discretion.

Reporting group title	Cohort 2: GDC-0853 High Dose

Reporting group description:

Participants of Cohort 2 received GDC-0853 high dose, orally twice daily for 12 weeks. Participants remained on a stable background therapy of MTX 15-25 mg/week (oral or parenteral; for participants entering the trial on MTX doses 15 mg/week, doses as low as 7.5 mg/week were allowed only if there was clear documentation in the medical record that higher doses were not tolerated or that the dose of MTX is the highest acceptable dose based on local clinical practice guidelines) and folic acid of at least 5 mg total dose weekly (or equivalent) as per investigator's discretion.

Reporting group title	Cohort 2: GDC-0853 Placebo

Reporting group description:

Participants of Cohort 2 received placebo matched to GDC-0853, orally twice daily for 12 weeks. Participants remained on a stable background therapy of MTX 15-25 mg/week (oral or parenteral; for

participants entering the trial on MTX doses 15 mg/week, doses as low as 7.5 mg/week were allowed only if there was clear documentation in the medical record that higher doses were not tolerated or that the dose of MTX is the highest acceptable dose based on local clinical practice guidelines) and folic acid of at least 5 mg total dose weekly (or equivalent) as per investigator's discretion.

Reporting group title	Cohort 1: GDC-0853 Low Dose + Adalimumab Placebo

Reporting group description:

Participants of Cohort 1 will receive GDC-0853 low dose, orally once daily along with placebo matched to adalimumab, subcutaneously Q2W starting on Day 1 for 12 weeks. Participants will remain on a stable background therapy of MTX 15-25 mg/week (oral or parenteral; for participants entering the trial on MTX doses 15 mg/week, doses as low as 7.5 mg/week are allowed only if there is clear documentation in the medical record that higher doses were not tolerated or that the dose of MTX is the highest acceptable dose based on local clinical practice guidelines) and folic acid of at least 5 mg total dose weekly (or equivalent) as per investigator's discretion.

Reporting group title	Cohort 1: GDC-0853 Mid Dose + Adalimumab Placebo

Reporting group description:

Participants of Cohort 1 will receive GDC-0853 mid dose, orally twice daily along with placebo matched to adalimumab, subcutaneously Q2W starting on Day 1 for 12 weeks. Participants will remain on a stable background therapy of MTX 15-25 mg/week (oral or parenteral; for participants entering the trial on MTX doses 15 mg/week, doses as low as 7.5 mg/week are allowed only if there is clear documentation in the medical record that higher doses were not tolerated or that the dose of MTX is the highest acceptable dose based on local clinical practice guidelines) and folic acid of at least 5 mg total dose weekly (or equivalent) as per investigator's discretion.

Reporting group title	Cohort 1: GDC-0853 High Dose + Adalimumab Placebo

Reporting group description:

Participants of Cohort 1 will receive GDC-0853 high dose, orally once daily along with placebo matched to adalimumab, subcutaneously every 2 weeks (Q2W) starting on Day 1 for 12 weeks. Participants will remain on a stable background therapy of MTX 15-25 milligrams per week (mg/week) (oral or parenteral; for participants entering the trial on MTX doses 15 mg/week, doses as low as 7.5 mg/week are allowed only if there is clear documentation in the medical record that higher doses were not tolerated or that the dose of MTX is the highest acceptable dose based on local clinical practice guidelines) and folic acid of at least 5 mg total dose weekly (or equivalent) as per investigator's discretion.

Reporting group title	Cohort 1: GDC-0853 Placebo + Adalimumab Placebo

Reporting group description:

Participants of Cohort 1 will receive placebo matched to GDC-0853, orally once daily along with placebo matched to adalimumab, subcutaneously Q2W starting on Day 1 for 12 weeks. Participants will remain on a stable background therapy of MTX 15-25 mg/week (oral or parenteral; for participants entering the trial on MTX doses 15 mg/week, doses as low as 7.5 mg/week are allowed only if there is clear documentation in the medical record that higher doses were not tolerated or that the dose of MTX is the highest acceptable dose based on local clinical practice guidelines) and folic acid of at least 5 mg total dose weekly (or equivalent) as per investigator's discretion.

Reporting group title	Cohort 1: GDC-0853 Placebo + Adalimumab

Reporting group description:

Participants of Cohort 1 will receive placebo matched to GDC-0853, orally once daily along with adalimumab, subcutaneously Q2W starting on Day 1 for 12 weeks. Participants will remain on a stable background therapy of MTX 15-25 mg/week (oral or parenteral; for participants entering the trial on MTX doses 15 mg/week, doses as low as 7.5 mg/week are allowed only if there is clear documentation in the medical record that higher doses were not tolerated or that the dose of MTX is the highest acceptable dose based on local clinical practice guidelines) and folic acid of at least 5 mg total dose weekly (or equivalent) as per investigator's discretion.

Reporting group title	Cohort 2: GDC-0853 High Dose

Reporting group description:

Participants of Cohort 2 will receive GDC-0853 high dose, orally twice daily for 12 weeks. Participants will remain on a stable background therapy of MTX 15-25 mg/week (oral or parenteral; for participants entering the trial on MTX doses 15 mg/week, doses as low as 7.5 mg/week are allowed only if there is clear documentation in the medical record that higher doses were not tolerated or that the dose of MTX is the highest acceptable dose based on local clinical practice guidelines) and folic acid of at least 5 mg total dose weekly (or equivalent) as per investigator's discretion.

Reporting group title	Cohort 2: GDC-0853 Placebo

Reporting group description:

Participants of Cohort 2 will receive placebo matched to GDC-0853, orally twice daily for 12 weeks. Participants will remain on a stable background therapy of MTX 15-25 mg/week (oral or parenteral; for participants entering the trial on MTX doses 15 mg/week, doses as low as 7.5 mg/week are allowed only

if there is clear documentation in the medical record that higher doses were not tolerated or that the dose of MTX is the highest acceptable dose based on local clinical practice guidelines) and folic acid of at least 5 mg total dose weekly (or equivalent) as per investigator's discretion.

Primary: Percentage of Participants Achieving American College of Rheumatology 50% (ACR50) Response at Day 84, Comparison Between GDC-0853 and Placebo (Cohort 1)

End point title	Percentage of Participants Achieving American College of Rheumatology 50% (ACR50) Response at Day 84, Comparison Between GDC-0853 and Placebo (Cohort 1)

End point description:

ACR50 response is defined as a ≥ 50% improvement (reduction) compared with baseline for both total joint count-68 joints (TJC68) and swollen joint count-66 joints (SJC66), as well as for three of the additional five ACR core set variables: Patient's Assessment of Pain over the previous 24 hours: using a Visual Analog Scale (VAS) left end of the line 0=no pain to right end of the line 100=unbearable pain; Patient's Global Assessment of Disease Activity and Physician's Global Assessment of Disease Activity over the previous 24 hours using a VAS where left end of the line 0=no disease activity to right end of the line 100=maximum disease activity; Health Assessment Questionnaire: 20 questions, 8 components: dressing/grooming, arising, eating, walking, hygiene, reach, grip and activities, 0=without difficulty to 3=unable to do; and acute-phase reactant [either C-reactive protein or Erythrocyte Sedimentation Rate].

End point type	Primary

End point timeframe:

Day 84

End point values	Cohort 1: GDC-0853 Low Dose + Adalimumab Placebo	Cohort 1: GDC-0853 Mid Dose + Adalimumab Placebo	Cohort 1: GDC-0853 High Dose + Adalimumab Placebo	Cohort 1: GDC-0853 Placebo + Adalimumab Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	109	110	110
Units: Percentage				
number (confidence interval 95%)	17.5 (5.72 to 29.28)	27.5 (19.14 to 35.91)	34.5 (25.66 to 43.43)	14.5 (7.96 to 21.13)

End point values	Cohort 1: GDC-0853 Placebo + Adalimumab			
Subject group type	Reporting group			
Number of subjects analysed	111			
Units: Percentage				
number (confidence interval 95%)	36.0 (27.10 to 44.97)			

Statistical analyses

Statistical analysis title	Week 12 Day 84
Comparison groups	Cohort 1: GDC-0853 Low Dose + Adalimumab Placebo v Cohort 1: GDC-0853 Placebo + Adalimumab Placebo
Number of subjects included in analysis	150
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.2503
Method	Cochran-Mantel-Haenszel
Parameter estimate	Weighted difference
Point estimate	8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.64
upper limit	21.64

Statistical analysis title	Week 12 Day 84
Comparison groups	Cohort 1: GDC-0853 Mid Dose + Adalimumab Placebo v Cohort 1: GDC-0853 Placebo + Adalimumab Placebo
Number of subjects included in analysis	219
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0164
Method	Cochran-Mantel-Haenszel
Parameter estimate	Weighted difference
Point estimate	12.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.37
upper limit	23.48

Statistical analysis title	Week 12 Day 84
Comparison groups	Cohort 1: GDC-0853 High Dose + Adalimumab Placebo v Cohort 1: GDC-0853 Placebo + Adalimumab Placebo
Number of subjects included in analysis	220
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0003
Method	Cochran-Mantel-Haenszel
Parameter estimate	Weighted difference
Point estimate	20
Confidence interval	
level	95 %
sides	2-sided
lower limit	9.21
upper limit	30.79

Primary: Percentage of Participants With Adverse Events

End point title	Percentage of Participants With Adverse Events[1]

End point description:

An Adverse event was considered any unfavorable and unintended sign, symptom, or disease associated with the use of the study drug, whether or not considered related to the study drug. Preexisting conditions that worsened during the study were reported as adverse events. A SAE was any experience that suggested a significant hazard, contraindication, side effect or precaution that: resulted in death, was life-threatening, required in-patient hospitalization or prolongation of existing hospitalization, resulted in persistent or significant disability/incapacity, was a congenital anomaly/birth defect or was medically significant. Safety population included all participants according to treatment administered.

End point type	Primary

End point timeframe:

Day 1 up to 8 weeks after last dose (up to Week 20)

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive statistics are presented for this measure. No statistical analyses were planned.

End point values	Cohort 1: GDC-0853 Low Dose + Adalimumab Placebo	Cohort 1: GDC-0853 Mid Dose + Adalimumab Placebo	Cohort 1: GDC-0853 High Dose + Adalimumab Placebo	Cohort 1: GDC-0853 Placebo + Adalimumab Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	109	110	110
Units: Percentage of participants				
number (not applicable)	37.5	42.2	50.9	45.5

End point values	Cohort 1: GDC-0853 Placebo + Adalimumab	Cohort 2: GDC-0853 High Dose	Cohort 2: GDC-0853 Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	111	49	49	
Units: Percentage of participants				
number (not applicable)	45.0	22.4	44.9	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving ACR50 Response at Day 84, Comparison Between GDC-0853 and Adalimumab (Cohort 1)

End point title	Percentage of Participants Achieving ACR50 Response at Day 84, Comparison Between GDC-0853 and Adalimumab (Cohort 1)

End point description:

ACR50 response is defined as a ≥ 50% improvement (reduction) compared with baseline for both total

joint count-68 joints (TJC68) and swollen joint count-66 joints (SJC66), as well as for three of the additional five ACR core set variables: Patient's Assessment of Pain over the previous 24 hours: using a Visual Analog Scale (VAS) left end of the line 0=no pain to right end of the line 100=unbearable pain; Patient's Global Assessment of Disease Activity and Physician's Global Assessment of Disease Activity over the previous 24 hours using a VAS where left end of the line 0=no disease activity to right end of the line 100=maximum disease activity; Health Assessment Questionnaire: 20 questions, 8 components: dressing/grooming, arising, eating, walking, hygiene, reach, grip and activities, 0=without difficulty to 3=unable to do; and acute-phase reactant [either C-reactive protein or Erythrocyte Sedimentation Rate].

End point type	Secondary

End point timeframe:

Day 84

End point values	Cohort 1: GDC-0853 Low Dose + Adalimumab Placebo	Cohort 1: GDC-0853 Mid Dose + Adalimumab Placebo	Cohort 1: GDC-0853 High Dose + Adalimumab Placebo	Cohort 1: GDC-0853 Placebo + Adalimumab Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	109	110	110
Units: Percentage				
number (confidence interval 95%)	17.5 (5.72 to 29.28)	27.5 (19.14 to 35.91)	34.5 (25.66 to 43.43)	14.5 (7.96 to 21.13)

End point values	Cohort 1: GDC-0853 Placebo + Adalimumab			
Subject group type	Reporting group			
Number of subjects analysed	111			
Units: Percentage				
number (confidence interval 95%)	36.0 (27.10 to 44.97)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving ACR50 Response at Day 84, Comparison Between GDC-0853 and Placebo (Cohort 2)

End point title	Percentage of Participants Achieving ACR50 Response at Day 84, Comparison Between GDC-0853 and Placebo (Cohort 2)

End point description:

ACR50 response is defined as a ≥ 50% improvement (reduction) compared with baseline for both total joint count-68 joints (TJC68) and swollen joint count-66 joints (SJC66), as well as for three of the additional five ACR core set variables: Patient's Assessment of Pain over the previous 24 hours: using a Visual Analog Scale (VAS) left end of the line 0=no pain to right end of the line 100=unbearable pain; Patient's Global Assessment of Disease Activity and Physician's Global Assessment of Disease Activity over the previous 24 hours using a VAS where left end of the line 0=no disease activity to right end of the line 100=maximum disease activity; Health Assessment Questionnaire: 20 questions, 8 components: dressing/grooming, arising, eating, walking, hygiene, reach, grip and activities, 0=without difficulty to 3=unable to do; and acute-phase reactant [either C-reactive protein or Erythrocyte

Sedimentation Rate].

End point type	Secondary

End point timeframe:

Day 84

End point values	Cohort 2: GDC-0853 High Dose	Cohort 2: GDC-0853 Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	48	50		
Units: Percentage				
number (confidence interval 95%)	25.0 (12.75 to 37.25)	12.0 (2.99 to 21.01)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving American College of Rheumatology 20% (ACR20) Response

End point title	Percentage of Participants Achieving American College of Rheumatology 20% (ACR20) Response

End point description:

ACR20 response is defined as a ≥ 20% improvement (reduction) compared with baseline for both total joint count-68 joints (TJC68) and swollen joint count-66 joints (SJC66), as well as for three of the additional five ACR core set variables: Patient's Assessment of Pain over the previous 24 hours: using a Visual Analog Scale (VAS) left end of the line 0=no pain to right end of the line 100=unbearable pain; Patient's Global Assessment of Disease Activity and Physician's Global Assessment of Disease Activity over the previous 24 hours using a VAS where left end of the line 0=no disease activity to right end of the line 100=maximum disease activity; Health Assessment Questionnaire: 20 questions, 8 components: dressing/grooming, arising, eating, walking, hygiene, reach, grip and activities, 0=without difficulty to 3=unable to do; and acute-phase reactant [either C-reactive protein or Erythrocyte Sedimentation Rate]

End point type	Secondary

End point timeframe:

Days 7, 14, 28, 56, and 84

End point values	Cohort 1: GDC-0853 Low Dose + Adalimumab Placebo	Cohort 1: GDC-0853 Mid Dose + Adalimumab Placebo	Cohort 1: GDC-0853 High Dose + Adalimumab Placebo	Cohort 1: GDC-0853 Placebo + Adalimumab Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	109	110	110
Units: Percentage				
number (confidence interval 95%)				
Week 1 Day 7	10.0 (.70 to 19.3)	14.7 (8.04 to 21.32)	13.6 (7.22 to 20.05)	10.0 (4.39 to 15.61)

Week 2 Day 14	12.5 (2.25 to 22.75)	19.3 (11.86 to 26.67)	27.3 (18.95 to 35.60)	16.4 (9.45 to 23.28)
Week 4 Day 28	30.0 (15.80 to 44.20)	34.9 (25.92 to 43.81)	41.8 (32.60 to 51.04)	25.5 (17.31 to 33.59)
Week 8 Day 56	50.0 (34.51 to 65.49)	52.3 (42.92 to 61.67)	58.2 (48.96 to 67.40)	37.3 (28.24 to 46.31)
Week 12 Day 84	60.0 (44.82 to 75.18)	56.0 (46.64 to 65.28)	59.1 (49.90 to 68.28)	36.4 (27.37 to 45.35)

End point values	Cohort 1: GDC-0853 Placebo + Adalimumab	Cohort 2: GDC-0853 High Dose	Cohort 2: GDC-0853 Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	111	48	50	
Units: Percentage				
number (confidence interval 95%)				
Week 1 Day 7	25.2 (17.15 to 33.30)	22.9 (11.03 to 34.81)	2.0 (0.00 to 5.88)	
Week 2 Day 14	48.6 (39.35 to 57.95)	25.0 (12.75 to 37.25)	10.0 (1.68 to 18.32)	
Week 4 Day 28	59.5 (50.33 to 68.59)	35.4 (21.89 to 48.95)	24.0 (12.16 to 35.84)	
Week 8 Day 56	71.2 (62.74 to 79.60)	47.9 (33.78 to 62.05)	18.0 (7.35 to 28.65)	
Week 12 Day 84	72.1 (63.73 to 80.42)	58.3 (44.39 to 72.28)	24.0 (12.16 to 35.84)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving American College of Rheumatology 50% (ACR50) Response

End point title	Percentage of Participants Achieving American College of Rheumatology 50% (ACR50) Response

End point description:

ACR50 response is defined as a ≥ 50% improvement (reduction) compared with baseline for both total joint count-68 joints (TJC68) and swollen joint count-66 joints (SJC66), as well as for three of the additional five ACR core set variables: Patient's Assessment of Pain over the previous 24 hours: using a Visual Analog Scale (VAS) left end of the line 0=no pain to right end of the line 100=unbearable pain; Patient's Global Assessment of Disease Activity and Physician's Global Assessment of Disease Activity over the previous 24 hours using a VAS where left end of the line 0=no disease activity to right end of the line 100=maximum disease activity; Health Assessment Questionnaire: 20 questions, 8 components: dressing/grooming, arising, eating, walking, hygiene, reach, grip and activities, 0=without difficulty to 3=unable to do; and acute-phase reactant [either C-reactive protein or Erythrocyte Sedimentation Rate].

End point type	Secondary

End point timeframe:

Days 7, 14, 28, 56, and 84

End point values	Cohort 1: GDC-0853 Low Dose + Adalimumab Placebo	Cohort 1: GDC-0853 Mid Dose + Adalimumab Placebo	Cohort 1: GDC-0853 High Dose + Adalimumab Placebo	Cohort 1: GDC-0853 Placebo + Adalimumab Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	109	110	110
Units: Percentage				
number (confidence interval 95%)				
Week 1 Day 7	2.5 (0.00 to 7.34)	2.8 (0.00 to 5.82)	3.6 (0.14 to 7.13)	2.7 (0.00 to 5.77)
Week 2 Day 14	0.0 (0.00 to 0.00)	1.8 (0.00 to 4.35)	7.3 (2.42 to 12.13)	2.7 (0.00 to 5.77)
Week 4 day 28	5.0 (0.00 to 11.75)	9.2 (3.76 to 14.59)	10.0 (4.39 to 15.61)	6.4 (1.80 to 10.93)
Week 8 Day 56	15.0 (3.93 to 26.07)	18.3 (11.08 to 25.62)	22.7 (14.9 to 30.56)	17.3 (10.21 to 24.34)
Week 12 Day 84	17.5 (5.72 to 29.28)	27.5 (19.14 to 35.91)	34.5 (25.66 to 43.43)	14.5 (7.96 to 21.13)

End point values	Cohort 1: GDC-0853 Placebo + Adalimumab	Cohort 2: GDC-0853 High Dose	Cohort 2: GDC-0853 Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	111	48	50	
Units: Percentage				
number (confidence interval 95%)				
Week 1 Day 7	4.5 (0.65 to 8.36)	6.3 (0.00 to 13.10)	2.0 (0.00 to 5.88)	
Week 2 Day 14	9.0 (3.68 to 14.34)	10.4 (1.77 to 19.06)	0.00 (0.00 to 0.00)	
Week 4 day 28	25.2 (17.15 to 33.30)	10.4 (1.77 to 19.06)	6.0 (0.00 to 12.58)	
Week 8 Day 56	32.4 (23.72 to 41.14)	22.9 (11.03 to 34.81)	10.0 (1.68 to 18.32)	
Week 12 Day 84	36.0 (27.10 to 44.97)	25.0 (12.75 to 37.25)	12.0 (2.99 to 21.01)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving American College of Rheumatology 70% (ACR70) Response

End point title	Percentage of Participants Achieving American College of Rheumatology 70% (ACR70) Response

End point description:

ACR70 response is defined as a ≥ 70% improvement (reduction) compared with Baseline for both total joint count-68 joints (TJC68) and swollen joint count-66 joints (SJC66), as well as for three of the additional five ACR core set variables: Patient's Assessment of Pain over the previous 24 hours: using a Visual Analog Scale (VAS) left end of the line 0=no pain to right end of the line 100=unbearable pain; Patient's Global Assessment of Disease Activity and Physician's Global Assessment of Disease Activity over the previous 24 hours using a VAS where left end of the line 0=no disease activity to right end of the line 100=maximum disease activity; Health Assessment Questionnaire: 20 questions, 8

components: dressing/grooming, arising, eating, walking, hygiene, reach, grip and activities, 0=without difficulty to 3=unable to do; and acute-phase reactant [either C-reactive protein or Erythrocyte Sedimentation Rate].

End point type	Secondary

End point timeframe:

Days 7, 14, 28, 56, and 84

End point values	Cohort 1: GDC-0853 Low Dose + Adalimumab Placebo	Cohort 1: GDC-0853 Mid Dose + Adalimumab Placebo	Cohort 1: GDC-0853 High Dose + Adalimumab Placebo	Cohort 1: GDC-0853 Placebo + Adalimumab Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	109	110	110
Units: Percentage				
number (confidence interval 95%)				
Week 1 Day 7	0.0 (0.00 to 0.00)	0.9 (0.00 to 2.71)	0.9 (0.00 to 2.68)	0.0 (0.00 to 0.00)
Week 2 Day 14	0.0 (0.00 to 0.00)	0.9 (0.00 to 2.71)	0.0 (0.00 to 0.00)	0.0 (0.00 to 0.00)
Week 4 Day 28	0.0 (0.00 to 0.00)	2.8 (0.00 to 5.82)	4.5 (0.65 to 8.44)	0.9 (0.00 to 2.68)
Week 8 Day 56	0.0 (0.00 to 0.00)	7.3 (2.44 to 12.24)	9.1 (3.72 to 14.46)	3.6 (0.14 to 7.13)
Week 12 Day 84	5.0 (0.00 to 11.75)	9.2 (3.76 to 14.59)	12.7 (6.50 to 18.96)	7.3 (2.42 to 12.13)

End point values	Cohort 1: GDC-0853 Placebo + Adalimumab	Cohort 2: GDC-0853 High Dose	Cohort 2: GDC-0853 Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	111	48	50	
Units: Percentage				
number (confidence interval 95%)				
Week 1 Day 7	0.0 (0.00 to 0.00)	0.0 (0.00 to 0.00)	0.0 (0.00 to 0.00)	
Week 2 Day 14	3.6 (0.14 to 7.07)	4.2 (0.00 to 9.82)	0.0 (0.00 to 0.00)	
Week 4 Day 28	6.3 (1.78 to 10.83)	2.1 (0.00 to 6.12)	2.0 (0.00 to 5.88)	
Week 8 Day 56	14.4 (7.88 to 20.95)	6.3 (0.00 to 13.10)	4.0 (0.00 to 9.43)	
Week 12 Day 84	18.0 (10.87 to 25.17)	14.6 (4.60 to 24.57)	4.0 (0.00 to 9.43)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Disease Activity Score from Baseline Based on 28-Joints Count and C-Reactive Protein (3 Variables) (DAS28-3 [CRP])

End point title	Change in Disease Activity Score from Baseline Based on 28-Joints Count and C-Reactive Protein (3 Variables) (DAS28-3 [CRP])

End point description:

The DAS28 score is a measure of the patient's disease activity calculated using the tender joint count (TJC) [28 joints], swollen joint count (SJC) [28 joints], patient's global assessment of disease activity [visual analog scale: 0=no disease activity to 100=maximum disease activity] and the erythrocyte sedimentation rate (ESR) for a total possible score of 0 to approximately 10. Scores below 2.6 indicate best disease control and scores above 5.1 indicate worse disease control. DAS28 Remission is defined as a DAS28 score < 2.6.

End point type	Secondary

End point timeframe:

Days 7, 14, 28, 56, and 84

End point values	Cohort 1: GDC-0853 Low Dose + Adalimumab Placebo	Cohort 1: GDC-0853 Mid Dose + Adalimumab Placebo	Cohort 1: GDC-0853 High Dose + Adalimumab Placebo	Cohort 1: GDC-0853 Placebo + Adalimumab Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	109	110	110
Units: Score on a scale				
arithmetic mean (standard deviation)				
Week 1 Day 7	-0.34 (± 0.60)	-0.35 (± 0.66)	-0.37 (± 0.80)	-0.33 (± 0.84)
Week 2 Day 14	-0.47 (± 0.72)	-0.63 (± 0.84)	-0.70 (± 0.80)	-.54 (± 0.90)
Week 4 Day 28	-0.75 (± 0.86)	-0.90 (± 0.96)	-0.91 (± 0.97)	-0.62 (± 1.04)
Week 8 Day 56	-1.14 (± 0.90)	-1.35 (± 1.12)	-1.37 (± 1.11)	-1.08 (± 1.19)
Week 12 Day 84	-1.30 (± 0.95)	-1.72 (± 1.11)	-1.70 (± 1.02)	-1.17 (± 1.24)

End point values	Cohort 1: GDC-0853 Placebo + Adalimumab	Cohort 2: GDC-0853 High Dose	Cohort 2: GDC-0853 Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	111	48	50	
Units: Score on a scale				
arithmetic mean (standard deviation)				
Week 1 Day 7	-0.92 (± 0.71)	-0.49 (± 0.84)	-0.36 (± 0.63)	
Week 2 Day 14	-1.09 (± 0.81)	-0.65 (± 0.87)	-0.45 (± 0.69)	
Week 4 Day 28	-1.45 (± 0.87)	-0.77 (± 0.90)	-0.44 (± 0.84)	
Week 8 Day 56	-1.75 (± 0.98)	-1.33 (± 0.98)	-0.56 (± 0.87)	
Week 12 Day 84	-1.87 (± 1.02)	-1.62 (± 1.15)	-0.86 (± 1.03)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Disease Activity Score from Baseline Based on 28-Joints Count and C-Reactive Protein (4 Variables) (DAS28-4 [CRP])

End point title	Change in Disease Activity Score from Baseline Based on 28-Joints Count and C-Reactive Protein (4 Variables) (DAS28-4 [CRP])

End point description:

The DAS28 score is a measure of the patient's disease activity calculated using the tender joint count (TJC) [28 joints], swollen joint count (SJC) [28 joints], patient's global assessment of disease activity [visual analog scale: 0=no disease activity to 100=maximum disease activity] and the erythrocyte sedimentation rate (ESR) for a total possible score of 0 to approximately 10. Scores below 2.6 indicate best disease control and scores above 5.1 indicate worse disease control. DAS28 Remission is defined as a DAS28 score < 2.6.

End point type	Secondary

End point timeframe:

Days 7, 14, 28, 56, and 84

End point values	Cohort 1: GDC-0853 Low Dose + Adalimumab Placebo	Cohort 1: GDC-0853 Mid Dose + Adalimumab Placebo	Cohort 1: GDC-0853 High Dose + Adalimumab Placebo	Cohort 1: GDC-0853 Placebo + Adalimumab Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	109	110	110
Units: Score on a scale				
arithmetic mean (standard deviation)				
Week 1 Day 7	-0.43 (± 0.67)	-0.48 (± 0.73)	-0.49 (± 0.86)	-0.37 (± 0.91)
Week 2 Day 14	-0.51 (± 0.85)	-0.77 (± 0.86)	-0.84 (± 0.86)	-0.57 (± 1.00)
Week 4 Day 28	-0.88 (± 0.90)	-1.06 (± 1.02)	-1.08 (± 1.03)	-0.65 (± 1.16)
Week 8 Day 56	-1.31 (± 0.91)	-1.56 (± 1.21)	-1.57 (± 1.16)	-1.20 (± 1.30)
Week 12 Day 84	-1.53 (± 0.95)	-1.97 (± 1.20)	-1.93 (± 1.11)	-1.33 (± 1.33)

End point values	Cohort 1: GDC-0853 Placebo + Adalimumab	Cohort 2: GDC-0853 High Dose	Cohort 2: GDC-0853 Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	111	48	50	
Units: Score on a scale				
arithmetic mean (standard deviation)				
Week 1 Day 7	-1.10 (± 0.75)	-0.63 (± 0.91)	-0.40 (± 0.69)	
Week 2 Day 14	-1.26 (± 0.89)	-0.81 (± 0.98)	-0.54 (± 0.80)	
Week 4 Day 28	-1.61 (± 0.94)	-0.95 (± 1.04)	-0.55 (± 0.94)	
Week 8 Day 56	-1.97 (± 1.03)	-1.51 (± 1.05)	-0.67 (± 1.01)	
Week 12 Day 84	-2.06 (± 1.08)	-1.83 (± 1.22)	-1.00 (± 1.11)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Disease Activity Score from Baseline Based on 28-Joints Count and Erythrocyte Sedimentation Rate (3 Variables) (DAS28-3 [ESR])

End point title	Change in Disease Activity Score from Baseline Based on 28-Joints Count and Erythrocyte Sedimentation Rate (3 Variables) (DAS28-3 [ESR])

End point description:

The DAS28 score is a measure of the patient's disease activity calculated using the tender joint count (TJC) [28 joints], swollen joint count (SJC) [28 joints], patient's global assessment of disease activity [visual analog scale: 0=no disease activity to 100=maximum disease activity] and the erythrocyte sedimentation rate (ESR) for a total possible score of 0 to approximately 10. Scores below 2.6 indicate best disease control and scores above 5.1 indicate worse disease control. DAS28 Remission is defined as a DAS28 score < 2.6.

End point type	Secondary

End point timeframe:

Days 7, 14, 28, 56, and 84

End point values	Cohort 1: GDC-0853 Low Dose + Adalimumab Placebo	Cohort 1: GDC-0853 Mid Dose + Adalimumab Placebo	Cohort 1: GDC-0853 High Dose + Adalimumab Placebo	Cohort 1: GDC-0853 Placebo + Adalimumab Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	109	110	110
Units: Score on a scale				
arithmetic mean (standard deviation)				
Week 1 Day 7	-0.35 (± 0.57)	-0.42 (± 0.65)	-0.39 (± 0.68)	-0.34 (± 0.86)
Week 2 Day 14	-0.60 (± 0.89)	-0.69 (± 0.84)	-0.68 (± 0.74)	-0.55 (± 0.92)
Week 4 Day 28	-0.88 (± 0.89)	-0.99 (± 0.98)	-0.97 (± 0.90)	-0.75 (± 1.02)
Week 8 Day 56	-1.25 (± 0.85)	-1.44 (± 1.14)	-1.40 (± 1.06)	-1.15 (± 1.19)
Week 12 Day 84	-1.51 (± 1.01)	-1.80 (± 1.25)	-1.80 (± 0.99)	-1.30 (± 1.22)

End point values	Cohort 1: GDC-0853 Placebo + Adalimumab	Cohort 2: GDC-0853 High Dose	Cohort 2: GDC-0853 Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	111	48	50	
Units: Score on a scale				
arithmetic mean (standard deviation)				
Week 1 Day 7	-0.72 (± 0.72)	-0.50 (± 0.73)	-0.31 (± 0.60)	
Week 2 Day 14	-1.02 (± 0.84)	-0.64 (± 0.81)	-0.51 (± 0.73)	
Week 4 Day 28	-1.47 (± 1.02)	-0.85 (± 0.81)	-0.50 (± 0.83)	
Week 8 Day 56	-1.74 (± 0.98)	-1.35 (± 0.96)	-0.70 (± 0.98)	
Week 12 Day 84	-1.85 (± 1.06)	-1.65 (± 1.06)	-0.94 (± 10.6)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Disease Activity Score from Baseline Based on 28-Joints Count and Erythrocyte Sedimentation Rate (4 Variables) (DAS28-4 [ESR])

End point title	Change in Disease Activity Score from Baseline Based on 28-Joints Count and Erythrocyte Sedimentation Rate (4 Variables) (DAS28-4 [ESR])

End point description:

The DAS28 score is a measure of the patient's disease activity calculated using the tender joint count (TJC) [28 joints], swollen joint count (SJC) [28 joints], patient's global assessment of disease activity [visual analog scale: 0=no disease activity to 100=maximum disease activity] and the erythrocyte sedimentation rate (ESR) for a total possible score of 0 to approximately 10. Scores below 2.6 indicate best disease control and scores above 5.1 indicate worse disease control. DAS28 Remission is defined as a DAS28 score < 2.6.

End point type	Secondary

End point timeframe:

Days 7, 14, 28, 56, and 84

End point values	Cohort 1: GDC-0853 Low Dose + Adalimumab Placebo	Cohort 1: GDC-0853 Mid Dose + Adalimumab Placebo	Cohort 1: GDC-0853 High Dose + Adalimumab Placebo	Cohort 1: GDC-0853 Placebo + Adalimumab Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	109	110	110
Units: Score on a scale				
arithmetic mean (standard deviation)				
Week 1 Day 7	-0.45 (± 0.63)	-0.54 (± 0.72)	-0.52 (± 0.77)	-0.37 (± 0.95)
Week 2 Day 14	-0.63 (± 0.98)	-0.85 (± 0.85)	-0.84 (± 0.82)	-0.58 (± 1.03)
Week 4 Day 28	-1.00 (± 0.95)	-1.16 (± 1.06)	-1.15 (± 0.98)	-0.79 (± 1.16)
Week 8 Day 56	-1.43 (± 0.88)	-1.67 (± 1.25)	-1.63 (± 1.14)	-1.29 (± 1.31)
Week 12 Day 84	-1.76 (± 1.04)	-2.06 (± 1.36)	-2.05 (± 1.08)	-1.46 (± 1.32)

End point values	Cohort 1: GDC-0853 Placebo + Adalimumab	Cohort 2: GDC-0853 High Dose	Cohort 2: GDC-0853 Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	111	48	50	
Units: Score on a scale				
arithmetic mean (standard deviation)				
Week 1 Day 7	-0.93 (± 0.76)	-0.65 (± 0.80)	-0.36 (± 0.66)	
Week 2 Day 14	-1.22 (± 0.94)	-0.81 (± 0.92)	-0.60 (± 0.84)	
Week 4 Day 28	-1.65 (± 1.11)	-1.04 (± 0.95)	-0.61 (± 0.96)	
Week 8 Day 56	-2.00 (± 1.06)	-1.54 (± 1.04)	-0.81 (± 1.12)	
Week 12 Day 84	-2.08 (± 1.14)	-1.89 (± 1.15)	-1.08 (± 1.17)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with DAS low Disease Activity

End point title	Percentage of Participants with DAS low Disease Activity

End point description:

The DAS28 score is a measure of the patient's disease activity calculated using the tender joint count (TJC) [28 joints], swollen joint count (SJC) [28 joints], patient's global assessment of disease activity [visual analog scale: 0=no disease activity to 100=maximum disease activity] and the erythrocyte sedimentation rate (ESR) for a total possible score of 0 to approximately 10. Scores below 2.6 indicate best disease control and scores above 5.1 indicate worse disease control. LDAS is defined as DAS28 ≤ 3.2

End point type	Secondary

End point timeframe:

Days 7, 14, 28, 56, and 84

End point values	Cohort 1: GDC-0853 Low Dose + Adalimumab Placebo	Cohort 1: GDC-0853 Mid Dose + Adalimumab Placebo	Cohort 1: GDC-0853 High Dose + Adalimumab Placebo	Cohort 1: GDC-0853 Placebo + Adalimumab Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	109	110	110
Units: Percentage of participants				
number (confidence interval 95%)				
Week 1 Day 7	0.0 (0.00 to 0.00)	0.9 (0.00 to 2.71)	1.8 (0.00 to 4.31)	0.0 (0.00 to 0.00)
Week 2 day 14	0.0 (0.00 to 0.00)	0.0 (0.00 to 0.00)	1.8 (0.00 to 4.31)	0.9 (0.00 to 2.68)
Week 4 Day 28	0.0 (0.00 to 0.00)	1.8 (0.00 to 4.35)	6.4 (1.80 to 10.93)	1.8 (0.00 to 4.31)
Week 8 Day 56	0.0 (0.00 to 0.00)	8.3 (3.09 to 13.42)	11.8 (5.79 to 17.85)	3.6 (0.14 to 7.13)
Week 12 Day 84	7.5 (0.00 to 15.66)	19.3 (11.86 to 26.67)	14.5 (7.86 to 21.13)	3.6 (0.14 to 7.13)

End point values	Cohort 1: GDC-0853 Placebo + Adalimumab	Cohort 2: GDC-0853 High Dose	Cohort 2: GDC-0853 Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	111	48	50	
Units: Percentage of participants				
number (confidence interval 95%)				
Week 1 Day 7	1.8 (0.00 to 4.28)	2.1 (0.00 to 6.12)	0.00 (0.00 to 0.00)	
Week 2 day 14	4.5 (0.65 to 8.36)	2.1 (0.00 to 6.12)	2.0 (0.00 to 5.88)	
Week 4 Day 28	11.7 (5.73 to 17.69)	2.1 (0.00 to 6.12)	0.0 (0.00 to 0.00)	
Week 8 Day 56	18.0 (10.87 to 25.17)	2.1 (0.00 to 6.12)	2.0 (0.00 to 5.88)	
Week 12 Day 84	17.1 (10.11 to 24.12)	14.6 (4.60 to 24.57)	4.0 (0.00 to 9.43)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with DAS Remission

End point title	Percentage of Participants with DAS Remission

End point description:

The DAS28 score is a measure of the patient's disease activity calculated using the tender joint count (TJC) [28 joints], swollen joint count (SJC) [28 joints], patient's global assessment of disease activity [visual analog scale: 0=no disease activity to 100=maximum disease activity] and the erythrocyte sedimentation rate (ESR) for a total possible score of 0 to approximately 10. Scores below 2.6 indicate best disease control and scores above 5.1 indicate worse disease control. DAS28 Remission is defined as a DAS28 score < 2.6

End point type	Secondary

End point timeframe:

Days 7, 14, 28, 56, and 84

End point values	Cohort 1: GDC-0853 Low Dose + Adalimumab Placebo	Cohort 1: GDC-0853 Mid Dose + Adalimumab Placebo	Cohort 1: GDC-0853 High Dose + Adalimumab Placebo	Cohort 1: GDC-0853 Placebo + Adalimumab Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	109	110	110
Units: Percentage of participants				
number (confidence interval 95%)				
Week 1 Day 7	0.0 (0.00 to 0.00)	0.0 (0.00 to 0.00)	0.0 (0.00 to 0.00)	0.0 (0.00 to 0.00)
Week 2 Day 14	0.0 (0.00 to 0.00)	0.0 (0.00 to 0.00)	0.9 (0.00 to 2.68)	0.0 (0.00 to 0.00)
Week 4 Day 28	0.0 (0.00 to 0.00)	0.0 (0.00 to 0.00)	1.8 (0.00 to 4.31)	0.9 (0.00 to 2.68)
Week 8 Day 56	0.0 (0.00 to 0.00)	3.7 (0.14 to 7.20)	4.5 (0.65 to 8.44)	1.8 (0.00 to 4.31)
Week 12 Day 84	2.5 (0.00 to 7.34)	7.3 (2.44 to 12.24)	8.2 (3.06 to 13.30)	3.6 (0.14 to 7.13)

End point values	Cohort 1: GDC-0853 Placebo + Adalimumab	Cohort 2: GDC-0853 High Dose	Cohort 2: GDC-0853 Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	111	48	50	
Units: Percentage of participants				
number (confidence interval 95%)				

Week 1 Day 7	0.0 (0.00 to 0.00)	2.1 (0.00 to 6.12)	0.0 (0.00 to 0.00)	
Week 2 Day 14	0.9 (0.00 to 2.66)	0.0 (0.00 to 0.00)	0.0 (0.00 to 0.00)	
Week 4 Day 28	4.5 (0.65 to 8.36)	0.0 (0.00 to 0.00)	0.0 (0.00 to 0.00)	
Week 8 Day 56	9.0 (3.68 to 14.34)	0.0 (0.00 to 0.00)	0.0 (0.00 to 0.00)	
Week 12 Day 84	9.0 (3.68 to 14.34)	4.2 (0.00 to 9.82)	4.0 (0.00 to 9.43)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Meeting the Boolean-based Remission Criteria

End point title	Percentage of Participants Meeting the Boolean-based Remission Criteria

End point description:

Boolean Remission is defined as Tender joint count less than 1, Swollen joint count less than 1, CRP less than 1 mg/dL, patient global assessment less than 1 (on 0 to 10 VAS scale).

End point type	Secondary

End point timeframe:

Days 7, 14, 28, 56, and 84

End point values	Cohort 1: GDC-0853 Low Dose + Adalimumab Placebo	Cohort 1: GDC-0853 Mid Dose + Adalimumab Placebo	Cohort 1: GDC-0853 High Dose + Adalimumab Placebo	Cohort 1: GDC-0853 Placebo + Adalimumab Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	109	110	110
Units: Percentage of participants				
number (confidence interval 95%)				
Week 1 Day 7	0.0 (0.00 to 0.00)	0.9 (0.00 to 2.76)	0.0 (0.00 to 0.00)	0.0 (0.00 to 0.00)
Week 2 Day 14	0.0 (0.00 to 0.00)	0.0 (0.00 to 0.00)	0.0 (0.00 to 0.00)	0.0 (0.00 to 0.00)
Week 4 Day 28	0.0 (0.00 to 0.00)	1.0 (0.00 to 2.81)	0.0 (0.00 to 0.00)	0.9 (0.00 to 2.73)
Week 8 Day 56	0.0 (0.00 to 0.00)	2.0 (0.00 to 4.70)	1.90 (0.00 to 4.56)	1.0 (0.00 to 2.86)
Week 12 Day 84	0.0 (0.00 to 0.00)	2.0 (0.00 to 4.84)	4.1 (0.17 to 8.08)	1.0 (0.00 to 2.89)

End point values	Cohort 1: GDC-0853 Placebo + Adalimumab	Cohort 2: GDC-0853 High Dose	Cohort 2: GDC-0853 Placebo	

Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	111	48	50	
Units: Percentage of participants				
number (confidence interval 95%)				
Week 1 Day 7	0.0 (0.00 to 0.00)	0.0 (0.00 to 0.00)	0.0 (0.00 to 0.00)	
Week 2 Day 14	0.0 (0.00 to 0.00)	0.0 (0.00 to 0.00)	0.0 (0.00 to 0.00)	
Week 4 Day 28	2.8 (0.00 to 5.82)	2.1 (0.00 to 6.25)	0.0 (0.00 to 0.00)	
Week 8 Day 56	3.7 (0.14 to 7.20)	0.0 (0.00 to 0.00)	0.0 (0.00 to 0.00)	
Week 12 Day 84	6.5 (1.84 to 11.12)	8.5 (0.53 to 16.49)	0.0 (0.00 to 6.53)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Clinical Disease Activity Index (CDAI)

End point title	Change from Baseline in Clinical Disease Activity Index (CDAI)

End point description:

Clinical Disease Activity Index is defined as CDAI= : SJC(28) + TJC(28) + PGA + MDG where TJC and SJC are the tender and swollen joint counts from 28 joints, PGA is the patient’s global assessment of disease activity (on a 0-10 scale) and MDG is physician global assessment of disease activity (on a 0-10 scale). The cutoff value for CDAI remission is <=2.8

End point type	Secondary

End point timeframe:

Baseline, Days 7, 14, 28, 56 and 84

End point values	Cohort 1: GDC-0853 Low Dose + Adalimumab Placebo	Cohort 1: GDC-0853 Mid Dose + Adalimumab Placebo	Cohort 1: GDC-0853 High Dose + Adalimumab Placebo	Cohort 1: GDC-0853 Placebo + Adalimumab Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	109	110	110
Units: Score on a scale				
arithmetic mean (standard deviation)				
Week 1 Day 7	-5.45 (± 7.69)	-6.70 (± 8.26)	-7.40 (± 9.97)	-4.71 (± 12.91)
Week 2 Day 14	-6.85 (± 11.10)	-10.33 (± 10.45)	-11.33 (± 10.47)	-7.44 (± 13.39)
Week 4 Day 28	-10.36 (± 10.88)	13.84 (± 12.11)	-13.78 (± 11.46)	-9.43 (± 14.77)
Week 8 Day 56	-14.76 (± 10.04)	-18.61 (± 13.48)	-18.10 (± 12.99)	-15.49 (± 15.74)
Week 12 Day 84	-16.99 (± 11.21)	-22.05 (± 12.19)	-22.10 (± 11.83)	-17.02 (± 16.24)

End point values	Cohort 1: GDC-0853 Placebo + Adalimumab	Cohort 2: GDC-0853 High Dose	Cohort 2: GDC-0853 Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	111	48	50	
Units: Score on a scale				
arithmetic mean (standard deviation)				
Week 1 Day 7	-9.64 (± 8.93)	-8.61 (± 10.67)	-5.26 (± 9.79)	
Week 2 Day 14	-13.44 (± 10.52)	-9.64 (± 12.17)	-7.70 (± 10.64)	
Week 4 Day 28	-17.74 (± 10.84)	-11.83 (± 11.08)	-7.49 (± 11.46)	
Week 8 Day 56	-21.36 (± 11.69)	-17.38 (± 12.39)	-7.57 (± 10.51)	
Week 12 Day 84	-22.22 (± 11.76)	-20.42 (± 13.20)	-12.23 (± 12.06)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Meeting the CDAI-based Remission Criteria

End point title	Percentage of Participants Meeting the CDAI-based Remission Criteria

End point description:

Clinical Disease Activity Index is defined as CDAI= : SJC(28) + TJC(28) + PGA + MDG where TJC and SJC are the tender and swollen joint counts from 28 joints, PGA is the patient’s global assessment of disease activity (on a 0-10 scale) and MDG is physician global assessment of disease activity (on a 0-10 scale). The cutoff value for CDAI remission is <=2.8.

End point type	Secondary

End point timeframe:

Days 7, 14, 28, 56, and 84

End point values	Cohort 1: GDC-0853 Low Dose + Adalimumab Placebo	Cohort 1: GDC-0853 Mid Dose + Adalimumab Placebo	Cohort 1: GDC-0853 High Dose + Adalimumab Placebo	Cohort 1: GDC-0853 Placebo + Adalimumab Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	109	110	110
Units: Percentage of participants				
number (confidence interval 95%)				
Week 1 Day 7	0.0 (0.00 to 0.00)	0.9 (0.00 to 2.71)	0.9 (0.00 to 2.68)	0.0 (0.00 to 0.00)
Week 2 Day 14	0.0 (0.00 to 0.00)	0.0 (0.00 to 0.00)	0.0 (0.0 to 0.00)	0.0 (0.00 to 0.00)

Week 4 Day 28	0.0 (0.00 to 0.00)	0.9 (0.00 to 2.71)	0.9 (0.00 to 2.68)	0.0 (0.00 to 0.00)
Week 8 Day 56	0.00 (0.0 to 0.00)	2.8 (0.0 to 5.82)	5.5 (1.21 to 9.70)	0.0 (0.00 to 0.00)
Week 12 Day 84	0.0 (0.00 to 0.00)	5.5 (1.22 to 9.79)	6.4 (1.80 to 10.93)	0.9 (0.00 to 2.68)

End point values	Cohort 1: GDC-0853 Placebo + Adalimumab	Cohort 2: GDC-0853 High Dose	Cohort 2: GDC-0853 Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	111	48	50	
Units: Percentage of participants				
number (confidence interval 95%)				
Week 1 Day 7	0.0 (0.00 to 0.00)	0.0 (0.00 to 0.00)	0.0 (0.00 to 0.00)	
Week 2 Day 14	1.8 (0.00 to 4.28)	0.0 (0.00 to 0.00)	0.0 (0.00 to 0.00)	
Week 4 Day 28	4.5 (0.65 to 8.36)	2.1 (0.0 to 6.12)	0.0 (0.00 to 0.00)	
Week 8 Day 56	7.2 (2.40 to 12.02)	4.2 (0.00 to 9.82)	0.0 (0.00 to 0.00)	
Week 12 Day 84	9.9 (4.35 to 15.47)	6.3 (0.00 to 13.10)	6.0 (0.00 to 12.58)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Simplified Disease Activity Index (SDAI)

End point title	Change from Baseline in Simplified Disease Activity Index (SDAI)

End point description:

Simplified Disease Activity Index (SDAI) is the numerical sum of five outcome parameters: TJC and SJC (based on a 28-joint assessment), PtGA and PhGA (based on 0-10 cm VAS, where 0 = no disease activity and 10 = worst disease activity), and CRP. SDAI total score ranges from 0 (no disease activity) to 86 (maximal disease activity), where higher scores represents higher disease activity. The SDAI =< 3.3 indicates disease remission, > 3.4 to 11 indicates low disease activity, > 11 to 26 indicates moderate disease activity, and > 26 indicates high disease activity

End point type	Secondary

End point timeframe:

Baseline, Days 7, 14, 28, 56 and 84

End point values	Cohort 1: GDC-0853 Low Dose + Adalimumab Placebo	Cohort 1: GDC-0853 Mid Dose + Adalimumab Placebo	Cohort 1: GDC-0853 High Dose + Adalimumab Placebo	Cohort 1: GDC-0853 Placebo + Adalimumab Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	109	110	110
Units: Score on a scale				
arithmetic mean (standard deviation)				
Week 1 Day 7	-5.36 (± 7.86)	-6.48 (± 8.87)	-6.99 (± 10.49)	-4.75 (± 13.25)
Week 2 Day 14	-6.50 (± 10.54)	-10.46 (± 10.97)	-11.44 (± 10.85)	-7.54 (± 13.74)
Week 4 Day 28	-10.53 (± 11.03)	-14.47 (± 12.41)	-14.21 (± 12.20)	-8.92 (± 15.17)
Week 8 Day 56	-15.25 (± 10.41)	-18.95 (± 13.80)	-18.97 (± 13.91)	-15.74 (± 16.18)
Week 12 Day 84	-17.54 (± 11.36)	-22.89 (± 12.52)	-23.24 (± 12.50)	-17.47 (± 16.70)

End point values	Cohort 1: GDC-0853 Placebo + Adalimumab	Cohort 2: GDC-0853 High Dose	Cohort 2: GDC-0853 Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	111	48	50	
Units: Score on a scale				
arithmetic mean (standard deviation)				
Week 1 Day 7	-10.86 (± 9.33)	-8.73 (± 11.21)	-5.37 (± 9.49)	
Week 2 Day 14	-14.39 (± 10.99)	-9.84 (± 12.29)	-8.13 (± 11.01)	
Week 4 Day 28	-18.87 (± 11.20)	-12.13 (± 11.13)	-7.74 (± 12.02)	
Week 8 Day 56	-22.62 (± 11.97)	-18.57 (± 12.80)	-7.82 (± 11.20)	
Week 12 Day 84	-23.33 (± 11.97)	-21.97 (± 13.78)	-12.92 (± 12.61)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Meeting the SDAI-based Remission Criteria

End point title	Percentage of Participants Meeting the SDAI-based Remission Criteria

End point description:

The SDAI was the numerical sum of five outcome parameter: SJC and TJC (based on a 28-joint assessment), PGA and MDG (based on 0-10 cm VAS, where 0 = no disease activity and 10 = worst disease activity), and CRP. The SDAI =< 3.3 indicates disease remission

End point type	Secondary

End point timeframe:

Days 7, 14, 28, 56, and 84

End point values	Cohort 1: GDC-0853 Low Dose + Adalimumab Placebo	Cohort 1: GDC-0853 Mid Dose + Adalimumab Placebo	Cohort 1: GDC-0853 High Dose + Adalimumab Placebo	Cohort 1: GDC-0853 Placebo + Adalimumab Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	109	110	110
Units: Percentage of participants				
number (confidence interval 95%)				
Week 1 Day 7	0.00 (0.00 to 0.00)	0.9 (0.00 to 2.71)	0.00 (0.00 to 0.00)	0.00 (0.00 to 0.00)
Week 2 Day 14	0.00 (0.00 to 0.00)	0.00 (0.00 to 0.00)	0.00 (0.00 to 0.00)	0.00 (0.00 to 0.00)
Week 4 Day 28	0.00 (0.00 to 0.00)	0.9 (0.00 to 2.71)	0.9 (0.00 to 2.68)	0.00 (0.00 to 0.00)
Week 8 Day 56	0.00 (0.00 to 0.00)	2.8 (0.00 to 5.82)	3.6 (0.14 to 7.13)	0.00 (0.00 to 0.00)
Week 12 Day 84	0.00 (0.00 to 0.00)	4.6 (0.66 to 8.51)	6.4 (1.80 to 10.93)	0.9 (0.00 to 2.68)

End point values	Cohort 1: GDC-0853 Placebo + Adalimumab	Cohort 2: GDC-0853 High Dose	Cohort 2: GDC-0853 Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	111	48	50	
Units: Percentage of participants				
number (confidence interval 95%)				
Week 1 Day 7	0.00 (0.00 to 0.00)	0.00 (0.00 to 0.00)	0.00 (0.00 to 0.00)	
Week 2 Day 14	1.8 (0.00 to 4.28)	0.00 (0.00 to 0.00)	0.00 (0.00 to 0.00)	
Week 4 Day 28	4.5 (0.65 to 8.36)	2.1 (0.00 to 6.12)	0.00 (0.00 to 0.00)	
Week 8 Day 56	6.3 (1.78 to 10.83)	0.00 (0.00 to 0.00)	0.00 (0.00 to 0.00)	
Week 12 Day 84	9.0 (3.68 to 14.34)	6.3 (0.00 to 13.10)	6.0 (0.00 to 12.58)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in 36-Item Short-Form Health Survey (SF-36) Version 2.0 (V2) Scores for Physical and Mental Components

End point title	Change from Baseline in 36-Item Short-Form Health Survey (SF-36) Version 2.0 (V2) Scores for Physical and Mental Components

End point description:

The 36-Item Short Form Health Survey (SF-36) is a questionnaire used to assess physical functioning

and is made up of eight domains: Physical Functioning, Role Physical, Bodily Pain, General Health, Vitality, Social Functioning, Role-Emotional and Mental Health.

End point type	Secondary

End point timeframe:

Day 84

End point values	Cohort 1: GDC-0853 Low Dose + Adalimumab Placebo	Cohort 1: GDC-0853 Mid Dose + Adalimumab Placebo	Cohort 1: GDC-0853 High Dose + Adalimumab Placebo	Cohort 1: GDC-0853 Placebo + Adalimumab Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	109	110	110
Units: Number on a scale				
arithmetic mean (standard deviation)				
Physical component score change:baseline-week 12	5.57 (± 5.98)	5.71 (± 6.85)	6.59 (± 7.54)	3.54 (± 6.81)
Mental component score change:baseline-week 12	7.04 (± 9.32)	4.89 (± 10.57)	6.92 (± 12.06)	4.29 (± 10.51)

End point values	Cohort 1: GDC-0853 Placebo + Adalimumab	Cohort 2: GDC-0853 High Dose	Cohort 2: GDC-0853 Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	111	48	50	
Units: Number on a scale				
arithmetic mean (standard deviation)				
Physical component score change:baseline-week 12	6.41 (± 6.43)	5.35 (± 7.48)	1.75 (± 6.39)	
Mental component score change:baseline-week 12	6.50 (± 10.79)	5.76 (± 10.22)	5.11 (± 10.10)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) Score

End point title	Change from Baseline in Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) Score

End point description:

The FACIT Fatigue questionnaire consists of 13 statements designed to measure the degree of fatigue experience by the patient in the previous 7 days. For each question, there are five possible responses: 0 (not at all), 1 (a little bit), 2 (somewhat), 3(quite a bit), 4 (very much). Statement 1 to 6 and 9 to 13 are worded so that higher scores correspond to greater fatigue, while statements 7 and 8 are worded so that higher scores correspond to less fatigue.

End point type	Secondary

End point timeframe:

Day 84

End point values	Cohort 1: GDC-0853 Low Dose + Adalimumab Placebo	Cohort 1: GDC-0853 Mid Dose + Adalimumab Placebo	Cohort 1: GDC-0853 High Dose + Adalimumab Placebo	Cohort 1: GDC-0853 Placebo + Adalimumab Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	109	110	110
Units: Score on a scale				
arithmetic mean (standard deviation)	9.00 (± 10.57)	8.21 (± 10.22)	8.95 (± 10.04)	7.08 (± 10.88)

End point values	Cohort 1: GDC-0853 Placebo + Adalimumab	Cohort 2: GDC-0853 High Dose	Cohort 2: GDC-0853 Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	111	48	50	
Units: Score on a scale				
arithmetic mean (standard deviation)	9.59 (± 9.02)	8.85 (± 9.57)	5.71 (± 9.24)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Tender/Painful Joint Count (68 Joint Count)

End point title	Change from Baseline in Tender/Painful Joint Count (68 Joint Count)

End point description:

Tender Joint Count: a total of 68 joints will be assessed for tenderness. Each joint is assessed for the presence/absence of tenderness.

End point type	Secondary

End point timeframe:

Days 7, 14, 28, 56, and 84

End point values	Cohort 1: GDC-0853 Low Dose + Adalimumab Placebo	Cohort 1: GDC-0853 Mid Dose + Adalimumab Placebo	Cohort 1: GDC-0853 High Dose + Adalimumab Placebo	Cohort 1: GDC-0853 Placebo + Adalimumab Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	109	110	110
Units: Score on a scale				
arithmetic mean (standard deviation)				
Week 1 Day 7	-2.79 (± 7.25)	-4.12 (± 8.14)	-3.33 (± 9.27)	-3.81 (± 10.85)

Week 2 Day 19	-4.33 (± 12.31)	-6.36 (± 10.88)	-5.91 (± 9.38)	-5.78 (± 11.50)
Week 4 Day 28	-6.00 (± 8.89)	-7.90 (± 11.28)	-6.84 (± 9.53)	-7.55 (± 12.97)
Week 8 Day 56	-9.72 (± 8.20)	-11.57 (± 12.18)	-9.75 (± 10.93)	-10.75 (± 14.37)
Week 12 Day 84	-10.33 (± 9.40)	-12.72 (± 12.05)	-11.49 (± 11.15)	-10.55 (± 14.37)

End point values	Cohort 1: GDC-0853 Placebo + Adalimumab	Cohort 2: GDC-0853 High Dose	Cohort 2: GDC-0853 Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	111	48	50	
Units: Score on a scale				
arithmetic mean (standard deviation)				
Week 1 Day 7	-5.58 (± 9.41)	-6.57 (± 8.66)	-3.06 (± 11.01)	
Week 2 Day 19	-8.62 (± 10.46)	-6.08 (± 8.53)	-3.92 (± 10.77)	
Week 4 Day 28	-11.61 (± 11.43)	-7.79 (± 7.93)	-4.40 (± 12.37)	
Week 8 Day 56	-14.12 (± 11.33)	-11.65 (± 10.34)	-4.60 (± 12.41)	
Week 12 Day 84	-15.49 (± 12.31)	-13.73 (± 12.81)	-7.14 (± 13.32)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Swollen Joint Count (66 Joint Count)

End point title	Change from Baseline in Swollen Joint Count (66 Joint Count)

End point description:

Swollen Joint Count: a total of 66 joints will be assessed for swelling. Each joint is assessed for the presence/absence of swelling

End point type	Secondary

End point timeframe:

Days 7, 14, 28, 56, and 84

End point values	Cohort 1: GDC-0853 Low Dose + Adalimumab Placebo	Cohort 1: GDC-0853 Mid Dose + Adalimumab Placebo	Cohort 1: GDC-0853 High Dose + Adalimumab Placebo	Cohort 1: GDC-0853 Placebo + Adalimumab Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	109	110	110
Units: Score on a scale				
arithmetic mean (standard deviation)				

Week 1 Day 7	-3.45 (± 6.02)	-2.89 (± 5.01)	-1.84 (± 5.19)	-3.35 (± 9.38)
Week 2 Day 14	-5.06 (± 5.14)	-4.78 (± 5.99)	-3.95 (± 6.44)	-4.23 (± 9.88)
Week 4 Day 28	-5.95 (± 6.09)	-6.33 (± 7.98)	-4.38 (± 4.55)	-5.47 (± 9.26)
Week 8 Day 56	-7.72 (± 7.44)	-8.06 (± 8.13)	-6.54 (± 5.78)	-7.41 (± 10.82)
Week 12 Day 84	-8.48 (± 7.01)	-8.89 (± 8.23)	-7.36 (± 5.88)	-8.26 (± 11.48)

End point values	Cohort 1: GDC-0853 Placebo + Adalimumab	Cohort 2: GDC-0853 High Dose	Cohort 2: GDC-0853 Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	111	48	50	
Units: Score on a scale				
arithmetic mean (standard deviation)				
Week 1 Day 7	-3.94 (± 5.33)	-3.45 (± 4.90)	-1.49 (± 4.49)	
Week 2 Day 14	-6.26 (± 5.98)	-3.29 (± 5.69)	-2.96 (± 6.27)	
Week 4 Day 28	-8.50 (± 6.39)	-4.21 (± 6.39)	-3.46 (± 5.62)	
Week 8 Day 56	-9.60 (± 6.94)	-6.81 (± 6.16)	-3.02 (± 7.76)	
Week 12 Day 84	-9.94 (± 6.91)	-7.65 (± 6.75)	-4.86 (± 5.84)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Patient Assessment Score of Arthritis Pain

End point title	Change from Baseline in Patient Assessment Score of Arthritis Pain

End point description:

Patient's Assessment of Pain over the previous 24 hours: using a Visual Analog Scale (VAS) left end of the line 0=no pain to right end of the line 100=unbearable pain

End point type	Secondary

End point timeframe:

Days 7, 14, 28, 56, and 84

End point values	Cohort 1: GDC-0853 Low Dose + Adalimumab Placebo	Cohort 1: GDC-0853 Mid Dose + Adalimumab Placebo	Cohort 1: GDC-0853 High Dose + Adalimumab Placebo	Cohort 1: GDC-0853 Placebo + Adalimumab Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	109	110	110
Units: Score on a scale				
arithmetic mean (standard deviation)				
Week 1 Day 7	-9.00 (± 18.66)	-9.20 (± 20.56)	-11.18 (± 21.64)	-4.12 (± 22.43)

Week 2 Day 14	-6.08 (± 21.64)	-12.16 (± 20.09)	-17.08 (± 23.46)	-8.22 (± 25.72)
Week 4 Day 28	-13.41 (± 16.79)	-15.75 (± 21.97)	-18.63 (± 24.87)	-10.08 (± 27.16)
Week 8 Day 56	-18.38 (± 19.35)	-23.21 (± 22.10)	-25.95 (± 27.50)	-16.37 (± 27.65)
Week 12 Day 84	-23.14 (± 21.14)	-26.48 (± 23.30)	-30.63 (± 28.49)	-17.88 (± 29.42)

End point values	Cohort 1: GDC-0853 Placebo + Adalimumab	Cohort 2: GDC-0853 High Dose	Cohort 2: GDC-0853 Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	111	48	50	
Units: Score on a scale				
arithmetic mean (standard deviation)				
Week 1 Day 7	-15.75 (± 18.71)	-11.94 (± 21.25)	-2.76 (± 18.24)	
Week 2 Day 14	-18.13 (± 17.71)	-15.08 (± 21.87)	-4.72 (± 17.64)	
Week 4 Day 28	-20.21 (± 21.97)	-16.64 (± 27.86)	-7.54 (± 23.80)	
Week 8 Day 56	-24.70 (± 22.23)	-21.21 (± 27.13)	-7.13 (± 25.73)	
Week 12 Day 84	-26.30 (± 23.87)	-26.49 (± 27.65)	-13.98 (± 25.32)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Patient Global Assessment Score of Arthritis Pain

End point title	Change from Baseline in Patient Global Assessment Score of Arthritis Pain
End point description: PGA is the patient’s global assessment of disease activity (on a 0-10 scale)	
End point type	Secondary
End point timeframe: Days 7, 14, 28, 56, and 84	

End point values	Cohort 1: GDC-0853 Low Dose + Adalimumab Placebo	Cohort 1: GDC-0853 Mid Dose + Adalimumab Placebo	Cohort 1: GDC-0853 High Dose + Adalimumab Placebo	Cohort 1: GDC-0853 Placebo + Adalimumab Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	109	110	110
Units: Score on a scale				

arithmetic mean (standard deviation)				
Week 1 Day 7	-9.00 (± 15.88)	-10.30 (± 20.82)	-11.82 (± 22.52)	-3.07 (± 20.83)
Week 2 Day 14	-5.50 (± 20.98)	-13.70 (± 19.63)	-14.84 (± 24.08)	-5.39 (± 26.13)
Week 4 Day 28	-12.11 (± 16.68)	16.10 (± 23.48)	-17.75 (± 22.73)	-6.36 (± 25.99)
Week 8 Day 56	-19.19 (± 16.88)	-24.06 (± 24.99)	-22.59 (± 26.81)	-14.19 (± 29.80)
Week 12 Day 84	-23.33 (± 22.03)	-26.67 (± 26.89)	-27.33 (± 27.33)	-16.87 (± 28.68)

End point values	Cohort 1: GDC-0853 Placebo + Adalimumab	Cohort 2: GDC-0853 High Dose	Cohort 2: GDC-0853 Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	111	48	50	
Units: Score on a scale				
arithmetic mean (standard deviation)				
Week 1 Day 7	-18.33 (± 20.81)	-13.15 (± 22.17)	-4.96 (± 19.18)	
Week 2 Day 14	-18.94 (± 22.33)	-15.46 (± 21.67)	-8.64 (± 19.43)	
Week 4 Day 28	-21.78 (± 25.53)	-18.26 (± 27.53)	-10.96 (± 21.54)	
Week 8 Day 56	-26.77 (± 25.80)	-21.17 (± 25.98)	-11.82 (± 21.66)	
Week 12 Day 84	-26.24 (± 27.02)	-25.55 (± 27.52)	-13.80 (± 22.17)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Physician's Global Assessment Score of Arthritis

End point title	Change from Baseline in Physician's Global Assessment Score of Arthritis
End point description:	
MDG is physician global assessment of disease activity (on a 0-10 scale).	
End point type	Secondary
End point timeframe:	
Days 7, 14, 28, 56, and 84	

End point values	Cohort 1: GDC-0853 Low Dose + Adalimumab Placebo	Cohort 1: GDC-0853 Mid Dose + Adalimumab Placebo	Cohort 1: GDC-0853 High Dose + Adalimumab Placebo	Cohort 1: GDC-0853 Placebo + Adalimumab Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	109	110	110
Units: Score on a scale				
arithmetic mean (standard deviation)				
Week 1 Day 7	-7.89 (± 13.16)	-10.68 (± 15.41)	-12.82 (± 17.03)	-5.85 (± 15.44)
Week 2 Day 14	-11.10 (± 15.65)	-15.86 (± 16.77)	-18.30 (± 19.04)	-9.01 (± 18.07)
Week 4 Day 28	-16.89 (± 19.06)	-22.02 (± 18.61)	-20.92 (± 17.71)	-14.01 (± 21.03)
Week 8 Day 56	-24.59 (± 15.06)	-28.52 (± 21.11)	-29.67 (± 20.01)	-20.87 (± 23.85)
Week 12 Day 84	-26.81 (± 16.20)	-32.43 (± 19.24)	-34.48 (± 19.49)	-23.19 (± 23.39)

End point values	Cohort 1: GDC-0853 Placebo + Adalimumab	Cohort 2: GDC-0853 High Dose	Cohort 2: GDC-0853 Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	111	48	50	
Units: Score on a scale				
arithmetic mean (standard deviation)				
Week 1 Day 7	-14.23 (± 16.13)	-9.57 (± 17.10)	-7.66 (± 18.33)	
Week 2 Day 14	-21.33 (± 19.61)	-14.23 (± 18.50)	-9.85 (± 17.55)	
Week 4 Day 28	-28.81 (± 19.34)	-17.70 (± 20.49)	-12.73 (± 20.42)	
Week 8 Day 56	-36.16 (± 21.82)	-22.40 (± 20.43)	-9.91 (± 19.67)	
Week 12 Day 84	-37.18 (± 21.02)	-30.82 (± 21.95)	-18.44 (± 21.86)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in C-Reactive Protein (CRP) Levels

End point title	Change from Baseline in C-Reactive Protein (CRP) Levels

End point description:

C-reactive protein is a biological marker of inflammation and is measured in nanograms per milliliter (ng/mL)

End point type	Secondary

End point timeframe:

Days 7, 14, 28, 56, and 84

End point values	Cohort 1: GDC-0853 Low Dose + Adalimumab Placebo	Cohort 1: GDC-0853 Mid Dose + Adalimumab Placebo	Cohort 1: GDC-0853 High Dose + Adalimumab Placebo	Cohort 1: GDC-0853 Placebo + Adalimumab Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	109	110	110
Units: (ng/mL) nanograms per milliliter				
arithmetic mean (standard deviation)				
Week 1 Day 7	0.14 (± 2.09)	0.30 (± 2.58)	0.22 (± 2.49)	0.01 (± 1.29)
Week 2 Day 14	0.27 (± 1.78)	-0.10 (± 1.92)	-0.21 (± 2.29)	-0.12 (± 1.53)
Week 4 Day 28	0.15 (± 2.45)	-0.25 (± 2.55)	-0.44 (± 2.30)	0.14 (± 2.00)
Week 8 Day 56	-0.49 (± 1.66)	-0.52 (± 1.83)	-0.89 (± 3.16)	-0.39 (± 1.64)
Week 12 Day 84	-0.59 (± 1.43)	-0.77 (± 1.89)	-1.30 (± 2.88)	-0.45 (± 1.71)

End point values	Cohort 1: GDC-0853 Placebo + Adalimumab	Cohort 2: GDC-0853 High Dose	Cohort 2: GDC-0853 Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	111	48	50	
Units: (ng/mL) nanograms per milliliter				
arithmetic mean (standard deviation)				
Week 1 Day 7	-1.21 (± 2.37)	-0.12 (± 2.60)	-0.10 (± 1.76)	
Week 2 Day 14	-0.93 (± 2.70)	-0.20 (± 2.38)	-0.25 (± 2.60)	
Week 4 Day 28	-1.11 (± 2.17)	-0.30 (± 2.58)	-0.24 (± 2.80)	
Week 8 Day 56	-1.14 (± 2.39)	-1.19 (± 2.18)	-0.26 (± 2.55)	
Week 12 Day 84	-1.03 (± 2.01)	-1.55 (± 2.35)	-0.56 (± 2.75)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Health Assessment Questionnaire-Disability Index (HAQ-DI) Score

End point title	Change from Baseline in Health Assessment Questionnaire-Disability Index (HAQ-DI) Score

End point description:

Health Assessment Questionnaire – Disability Index (HAQ-DI): The Stanford Health Assessment Questionnaire disability index is a patient reported questionnaire specific for RA. It consists of 20 questions referring to eight component

End point type	Secondary

End point timeframe:

Days 7, 14, 28, 56, and 84

End point values	Cohort 1: GDC-0853 Low Dose + Adalimumab Placebo	Cohort 1: GDC-0853 Mid Dose + Adalimumab Placebo	Cohort 1: GDC-0853 High Dose + Adalimumab Placebo	Cohort 1: GDC-0853 Placebo + Adalimumab Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	109	110	110
Units: Score on a scale				
arithmetic mean (standard deviation)				
Week 1 Day 7	-0.20 (± 0.37)	-0.15 (± 0.35)	-0.22 (± 0.48)	-0.10 (± 0.38)
Week 2 Day 14	-0.24 (± 0.39)	-0.23 (± 0.46)	-0.28 (± 0.50)	-0.17 (± 0.45)
Week 4 Day 28	-0.34 (± 0.47)	-0.32 (± 0.48)	-0.40 (± 0.50)	-0.19 (± 0.56)
Week 8 Day 56	-0.49 (± 0.47)	-0.44 (± 0.56)	-0.56 (± 0.55)	-0.40 (± 0.64)
Week 12 Day 84	-0.51 (± 0.57)	-0.57 (± 0.57)	-0.65 (± 0.60)	-0.35 (± 0.68)

End point values	Cohort 1: GDC-0853 Placebo + Adalimumab	Cohort 2: GDC-0853 High Dose	Cohort 2: GDC-0853 Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	111	48	50	
Units: Score on a scale				
arithmetic mean (standard deviation)				
Week 1 Day 7	-0.26 (± 0.42)	-0.19 (± 0.36)	-0.14 (± 0.46)	
Week 2 Day 14	-0.35 (± 0.47)	-0.23 (± 0.45)	-0.13 (± 0.49)	
Week 4 Day 28	-0.50 (± 0.50)	-0.23 (± 0.42)	-0.17 (± 0.44)	
Week 8 Day 56	-0.60 (± 0.55)	-0.45 (± 0.50)	-0.23 (± 0.55)	
Week 12 Day 84	-0.65 (± 0.61)	-0.53 (± 0.61)	-0.30 (± 0.62)	

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Concentration Time Curve From Time 0 to Time 24 of GDC-0853 at Steady State (AUC0-24,ss)

End point title	Area Under the Concentration Time Curve From Time 0 to Time 24 of GDC-0853 at Steady State (AUC0-24,ss)

End point description:

The Pharmacokinetics (PK) evaluation may include, but will not be limited to, plasma GDC-0853 concentrations and population PK model estimated PK exposures (area under the plasma concentration-time curve [AUC]. AUC was measured in Nanograms(ng) per millilitre(mL)*hour (hr)

End point type	Secondary

End point timeframe:

Pre-dose (0 hours) up to 10 hours post-dose on Day 28

End point values	Cohort 1: GDC-0853 Low Dose + Adalimumab Placebo	Cohort 1: GDC-0853 Mid Dose + Adalimumab Placebo	Cohort 1: GDC-0853 High Dose + Adalimumab Placebo	Cohort 2: GDC-0853 High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	39	106	108	48
Units: Ng/mL*(hr)				
arithmetic mean (standard deviation)	1170 (± 1600)	2910 (± 3180)	9380 (± 4860)	9890 (± 5480)

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Plasma Concentration of GDC-0853 at Steady State (Cmax,ss)

End point title	Maximum Observed Plasma Concentration of GDC-0853 at Steady State (Cmax,ss)

End point description:

Cmax is the maximum (peak) plasma concentration over the dosing interval at steady state (ss)

End point type	Secondary

End point timeframe:

Pre-dose (0 hours) up to 10 hours post-dose on Day 28

End point values	Cohort 1: GDC-0853 Low Dose + Adalimumab Placebo	Cohort 1: GDC-0853 Mid Dose + Adalimumab Placebo	Cohort 1: GDC-0853 High Dose + Adalimumab Placebo	Cohort 2: GDC-0853 High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	39	106	108	48
Units: Nanogram per Milliliter (ng/mL)				
arithmetic mean (standard deviation)	110 (± 116)	280 (± 223)	591 (± 282)	621 (± 302)

Statistical analyses

No statistical analyses for this end point

Secondary: Minimum Observed Plasma Concentration of GDC-0853 at Steady State (Cmin,ss)

End point title	Minimum Observed Plasma Concentration of GDC-0853 at Steady State (Cmin,ss)

End point description:

Cmin is the minimum concentration over the dosing interval at steady state (ss)

End point type	Secondary

End point timeframe:

Pre-dose (0 hours) up to 10 hours post-dose on Day 28

End point values	Cohort 1: GDC-0853 Low Dose + Adalimumab Placebo	Cohort 1: GDC-0853 Mid Dose + Adalimumab Placebo	Cohort 1: GDC-0853 High Dose + Adalimumab Placebo	Cohort 2: GDC-0853 High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	39	106	108	48
Units: Nanogram per Milliliter (ng/mL)				
arithmetic mean (standard deviation)	22.4 (± 41.0)	54.7 (± 83.4)	250 (± 146)	263 (± 170)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From randomization to end of study (approximately 22 months)

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups

Reporting group title	Cohort 1: GDC-0853 Low Dose + Adalimumab Placebo

Reporting group description:

Participants of Cohort 1 will receive GDC-0853 low dose, orally once daily along with placebo matched to adalimumab, subcutaneously Q2W starting on Day 1 for 12 weeks. Participants will remain on a stable background therapy of MTX 15-25 mg/week (oral or parenteral; for participants entering the trial on MTX doses 15 mg/week, doses as low as 7.5 mg/week are allowed only if there is clear documentation in the medical record that higher doses were not tolerated or that the dose of MTX is the highest acceptable dose based on local clinical practice guidelines) and folic acid of at least 5 mg total dose weekly (or equivalent) as per investigator's discretion.

Reporting group title	Cohort 1: GDC-0853 Mid Dose + Adalimumab Placebo

Reporting group description:

Participants of Cohort 1 will receive GDC-0853 mid dose, orally twice daily along with placebo matched to adalimumab, subcutaneously Q2W starting on Day 1 for 12 weeks. Participants will remain on a stable background therapy of MTX 15-25 mg/week (oral or parenteral; for participants entering the trial on MTX doses 15 mg/week, doses as low as 7.5 mg/week are allowed only if there is clear documentation in the medical record that higher doses were not tolerated or that the dose of MTX is the highest acceptable dose based on local clinical practice guidelines) and folic acid of at least 5 mg total dose weekly (or equivalent) as per investigator's discretion.

Reporting group title	Cohort 1: GDC-0853 High Dose + Adalimumab Placebo

Reporting group description:

Participants of Cohort 1 will receive GDC-0853 high dose, orally once daily along with placebo matched to adalimumab, subcutaneously every 2 weeks (Q2W) starting on Day 1 for 12 weeks. Participants will remain on a stable background therapy of MTX 15-25 milligrams per week (mg/week) (oral or parenteral; for participants entering the trial on MTX doses 15 mg/week, doses as low as 7.5 mg/week are allowed only if there is clear documentation in the medical record that higher doses were not tolerated or that the dose of MTX is the highest acceptable dose based on local clinical practice guidelines) and folic acid of at least 5 mg total dose weekly (or equivalent) as per investigator's discretion.

Reporting group title	Cohort 1: GDC-0853 Placebo + Adalimumab Placebo

Reporting group description:

Participants of Cohort 1 will receive placebo matched to GDC-0853, orally once daily along with placebo matched to adalimumab, subcutaneously Q2W starting on Day 1 for 12 weeks. Participants will remain on a stable background therapy of MTX 15-25 mg/week (oral or parenteral; for participants entering the trial on MTX doses 15 mg/week, doses as low as 7.5 mg/week are allowed only if there is clear documentation in the medical record that higher doses were not tolerated or that the dose of MTX is the highest acceptable dose based on local clinical practice guidelines) and folic acid of at least 5 mg total dose weekly (or equivalent) as per investigator's discretion.

Reporting group title	Cohort 1: GDC-0853 Placebo + Adalimumab

Reporting group description:

Participants of Cohort 1 will receive placebo matched to GDC-0853, orally once daily along with adalimumab, subcutaneously Q2W starting on Day 1 for 12 weeks. Participants will remain on a stable background therapy of MTX 15-25 mg/week (oral or parenteral; for participants entering the trial on MTX doses 15 mg/week, doses as low as 7.5 mg/week are allowed only if there is clear documentation in the medical record that higher doses were not tolerated or that the dose of MTX is the highest acceptable dose based on local clinical practice guidelines) and folic acid of at least 5 mg total dose weekly (or equivalent) as per investigator's discretion.

Reporting group title	Cohort 2: GDC-0853 High Dose

Reporting group description:

Participants of Cohort 2 will receive GDC-0853 high dose, orally twice daily for 12 weeks. Participants

will remain on a stable background therapy of MTX 15-25 mg/week (oral or parenteral; for participants entering the trial on MTX doses 15 mg/week, doses as low as 7.5 mg/week are allowed only if there is clear documentation in the medical record that higher doses were not tolerated or that the dose of MTX is the highest acceptable dose based on local clinical practice guidelines) and folic acid of at least 5 mg total dose weekly (or equivalent) as per investigator's discretion.

Reporting group title	Cohort 2: GDC-0853 Placebo

Reporting group description:

Participants of Cohort 2 will receive placebo matched to GDC-0853, orally twice daily for 12 weeks. Participants will remain on a stable background therapy of MTX 15-25 mg/week (oral or parenteral; for participants entering the trial on MTX doses 15 mg/week, doses as low as 7.5 mg/week are allowed only if there is clear documentation in the medical record that higher doses were not tolerated or that the dose of MTX is the highest acceptable dose based on local clinical practice guidelines) and folic acid of at least 5 mg total dose weekly (or equivalent) as per investigator's discretion.

Serious adverse events	Cohort 1: GDC-0853 Low Dose + Adalimumab Placebo	Cohort 1: GDC-0853 Mid Dose + Adalimumab Placebo	Cohort 1: GDC-0853 High Dose + Adalimumab Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 40 (0.00%)	1 / 109 (0.92%)	3 / 110 (2.73%)
number of deaths (all causes)	0	0	1
number of deaths resulting from adverse events			
Cardiac disorders			
MYOCARDIAL INFARCTION			
subjects affected / exposed	0 / 40 (0.00%)	0 / 109 (0.00%)	1 / 110 (0.91%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Nervous system disorders			
SEIZURE			
subjects affected / exposed	0 / 40 (0.00%)	0 / 109 (0.00%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
SMALL INTESTINAL DISORDERS			
subjects affected / exposed	0 / 40 (0.00%)	0 / 109 (0.00%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
CHRONIC OBSTRUCTIVE PULMONARY DISEASE			
subjects affected / exposed	0 / 40 (0.00%)	0 / 109 (0.00%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

PLEURAL EFFUSION			
subjects affected / exposed	0 / 40 (0.00%)	0 / 109 (0.00%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
CELLULITS			
subjects affected / exposed	0 / 40 (0.00%)	0 / 109 (0.00%)	1 / 110 (0.91%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA			
subjects affected / exposed	0 / 40 (0.00%)	1 / 109 (0.92%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PYELONEPHRITIS OBSTRUCTION			
subjects affected / exposed	0 / 40 (0.00%)	0 / 109 (0.00%)	1 / 110 (0.91%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Cohort 1: GDC-0853 Placebo + Adalimumab Placebo	Cohort 1: GDC-0853 Placebo + Adalimumab	Cohort 2: GDC-0853 High Dose
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 110 (0.91%)	2 / 111 (1.80%)	0 / 49 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Cardiac disorders			
MYOCARDIAL INFARCTION			
subjects affected / exposed	0 / 110 (0.00%)	0 / 111 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
SEIZURE			
subjects affected / exposed	0 / 110 (0.00%)	1 / 111 (0.90%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
SMALL INTESTINAL DISORDERS			

subjects affected / exposed	0 / 110 (0.00%)	1 / 111 (0.90%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
CHRONIC OBSTRUCTIVE PULMONARY DISEASE			
subjects affected / exposed	1 / 110 (0.91%)	0 / 111 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PLEURAL EFFUSION			
subjects affected / exposed	1 / 110 (0.91%)	0 / 111 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
CELLULITS			
subjects affected / exposed	0 / 110 (0.00%)	0 / 111 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA			
subjects affected / exposed	1 / 110 (0.91%)	0 / 111 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PYELONEPHRITIS OBSTRUCTION			
subjects affected / exposed	0 / 110 (0.00%)	0 / 111 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Cohort 2: GDC-0853 Placebo		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 49 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Cardiac disorders			
MYOCARDIAL INFARCTION			

subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
SEIZURE			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
SMALL INTESTINAL DISORDERS			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
CHRONIC OBSTRUCTIVE PULMONARY DISEASE			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
PLEURAL EFFUSION			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
CELLULITS			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
PNEUMONIA			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
PYELONEPHRITIS OBSTRUCTION			

subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Cohort 1: GDC-0853 Low Dose + Adalimumab Placebo	Cohort 1: GDC-0853 Mid Dose + Adalimumab Placebo	Cohort 1: GDC-0853 High Dose + Adalimumab Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 40 (22.50%)	18 / 109 (16.51%)	11 / 110 (10.00%)
Investigations			
ALANINE AMINOTRANFERASE INCREASED			
subjects affected / exposed	2 / 40 (5.00%)	5 / 109 (4.59%)	4 / 110 (3.64%)
occurrences (all)	3	5	4
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	2 / 40 (5.00%)	4 / 109 (3.67%)	3 / 110 (2.73%)
occurrences (all)	2	4	4
Nervous system disorders			
HEADACHE			
subjects affected / exposed	2 / 40 (5.00%)	4 / 109 (3.67%)	5 / 110 (4.55%)
occurrences (all)	2	5	5
Gastrointestinal disorders			
NAUSEA			
subjects affected / exposed	2 / 40 (5.00%)	5 / 109 (4.59%)	3 / 110 (2.73%)
occurrences (all)	2	5	3
VOMITING			
subjects affected / exposed	2 / 40 (5.00%)	1 / 109 (0.92%)	0 / 110 (0.00%)
occurrences (all)	2	1	0
Psychiatric disorders			
ANXIETY			
subjects affected / exposed	0 / 40 (0.00%)	0 / 109 (0.00%)	0 / 110 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
UPPER RESPIRATORY TRACT INFECTION			

subjects affected / exposed	1 / 40 (2.50%)	3 / 109 (2.75%)	3 / 110 (2.73%)
occurrences (all)	1	3	3
URINARY TRACT INFECTION			
subjects affected / exposed	2 / 40 (5.00%)	2 / 109 (1.83%)	0 / 110 (0.00%)
occurrences (all)	3	3	0

Non-serious adverse events	Cohort 1: GDC-0853 Placebo + Adalimumab Placebo	Cohort 1: GDC-0853 Placebo + Adalimumab	Cohort 2: GDC-0853 High Dose
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 110 (13.64%)	16 / 111 (14.41%)	3 / 49 (6.12%)
Investigations			
ALANINE AMINOTRANFERASE INCREASED			
subjects affected / exposed	1 / 110 (0.91%)	1 / 111 (0.90%)	0 / 49 (0.00%)
occurrences (all)	1	1	0
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	1 / 110 (0.91%)	1 / 111 (0.90%)	0 / 49 (0.00%)
occurrences (all)	1	1	0
Nervous system disorders			
HEADACHE			
subjects affected / exposed	5 / 110 (4.55%)	0 / 111 (0.00%)	0 / 49 (0.00%)
occurrences (all)	5	0	0
Gastrointestinal disorders			
NAUSEA			
subjects affected / exposed	5 / 110 (4.55%)	1 / 111 (0.90%)	3 / 49 (6.12%)
occurrences (all)	6	1	4
VOMITING			
subjects affected / exposed	0 / 110 (0.00%)	1 / 111 (0.90%)	0 / 49 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
ANXIETY			
subjects affected / exposed	0 / 110 (0.00%)	0 / 111 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	2 / 110 (1.82%)	6 / 111 (5.41%)	0 / 49 (0.00%)
occurrences (all)	2	6	0
URINARY TRACT INFECTION			

subjects affected / exposed	2 / 110 (1.82%)	8 / 111 (7.21%)	0 / 49 (0.00%)
occurrences (all)	2	10	0

Non-serious adverse events	Cohort 2: GDC-0853 Placebo		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 49 (14.29%)		
Investigations			
ALANINE AMINOTRANFERASE INCREASED			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences (all)	0		
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
HEADACHE			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
NAUSEA			
subjects affected / exposed	1 / 49 (2.04%)		
occurrences (all)	1		
VOMITING			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
ANXIETY			
subjects affected / exposed	3 / 49 (6.12%)		
occurrences (all)	3		
Infections and infestations			
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences (all)	0		
URINARY TRACT INFECTION			
subjects affected / exposed	3 / 49 (6.12%)		
occurrences (all)	3		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 August 2016	The secondary efficacy objective to assess Boolean- and SDAI-based remission was clarified. Patients were excluded if treatment with methotrexate or folic acid was contraindicated. The timing of the planned interim analysis was clarified by specifying that the analysis was performed after 150 patients had completed the 12-week assessment.
10 March 2017	The initiation of Cohort 2 was no longer to be gated on the IA. The decision to open Cohort 2 was based on evidence for activity of BTK inhibition in patients with RA, as demonstrated by another BTK inhibitor.The population for Cohort 2 was broadened to also include those who may have had intolerance to 1 or 2 TNF inhibitors and who may have also had exposure to no more than one non-TNF inhibitor biologic. The size of Cohort 2 was expanded.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported