Long-Term Study of the Effects of Navarixin (SCH 527123, MK-7123) in Participants With Moderate to Severe COPD (MK-7123-019)

This study has been terminated.

Sponsor:
Merck Sharp & Dohme Corp.

Information provided by (Responsible Party):
Merck Sharp & Dohme Corp.

ClinicalTrials.gov Identifier:
NCT01006616

First received: October 1, 2009
Last updated: April 24, 2015
Last verified: April 2015
History of Changes

Full Text View | Tabular View | Study Results | Disclaimer | How to Read a Study Record

Purpose

Neutrophils are thought to play an important role in the pathophysiology of chronic obstructive pulmonary disease (COPD). Navarixin (SCH 527123, MK-7123) is an antagonist of the cysteine-X-cysteine chemokine receptor 2 (CXCR2) and is thought to reduce neutrophil migration to the diseased lung. It is theorized that reducing neutrophil migration to the diseased lung will improve a participant's symptoms and the natural history of the disease.

The study will consist of a 2-week screening period followed by a 2-year (104-week) double-blind treatment period. The 2-year Treatment Period will be made up of two phases: a 26-week (6-month) dose range-finding phase with 3 active arms and 1 placebo arm (Period 1), followed by a 78-week (18-month) long-term safety and efficacy phase (Period 2). Participants participating in the original 6-month study (Period 1) may elect not to continue into the 18-month extension study (Period 2).

Hypothesis: navarixin, 50 mg, or the highest remaining dose if the 50-mg dose is discontinued, is superior to placebo with respect to improving airflow.

Condition	Intervention	Phase
COPD	Drug: Navarixin Drug: Placebo Drug: Rescue medication	Phase 2

Study Type: Interventional
Study Design: Allocation: Randomized
Endpoint Classification: Efficacy Study
Intervention Model: Parallel Assignment
Masking: Double Blind (Subject, Investigator)
Primary Purpose: Treatment

Official Title: A 2-Year, Dose Range-Finding, Adaptive-Design Study of the Effects of SCH 527123 in Subjects With Moderate to Severe COPD

Further study details as provided by Merck Sharp & Dohme Corp.:

Primary Outcome Measures:

- Change From Baseline in Post-bronchodilator Forced Expiratory Volume in 1 Second (FEV1) (Period 1) [Time Frame: Baseline and Week 26] [Designated as safety issue: No]

  FEV1, as measured in liters by spirometry, is the amount of air expired in 1 second. Participants were assessed for post-bronchodilator FEV1 30 minutes after bronchodilator administration (4 puffs of albuterol/salbutamol or equivalent separated by 30-second intervals) (reversibility test) at Baseline and Week 26.

- Percentage of Participants With an Adverse Event (AE) Related to a Blood Absolute Neutrophil Count (ANC) of Less Than 1.5x10^9 Cells/L [Time Frame: Up to 104 weeks] [Designated as safety issue: Yes]

  The percentage of participants who experienced an AE related to an ANC of less than 1.5x10^9 cells/L at one or more visits during the first 26 weeks, the first 52 weeks and the first 104 weeks was to be calculated.

Secondary Outcome Measures:

- Change From Baseline in Post-bronchodilator FEV1 (Period 2) [Time Frame: Baseline and Week 52, Week 104] [Designated as safety issue: No]

  FEV1, as measured in liters by spirometry, is the amount of air expired in 1 second. Participants were to be assessed for post-bronchodilator FEV1 30 minutes after bronchodilator administration (4 puffs of albuterol/salbutamol or equivalent separated by 30-second intervals) (reversibility test) at Baseline, Week 52 and Week 104.

- Number of Participants With a Moderate to Severe Chronic Obstructive Pulmonary Disease (COPD) Exacerbation [Time Frame: Up to 26 , 52 and 104 weeks] [Designated as safety issue: No]

  COPD exacerbation is defined as any deterioration of symptoms that leads to an increase in bronchodilator use on 2 or more consecutive days, or administration (at investigator's discretion) of antibiotics and/or systemic corticosteroids (above participant's usual dose), or an unscheduled COPD-related doctor visit, hospitalization or emergency room treatment. The numbers of participants who experienced at least one moderate to severe COPD exacerbation during the first 26 weeks, the first 52 weeks and the first 104 weeks of treatment were to be summarized.

- Percentage of Participants With a Moderate to Severe COPD Exacerbation [Time Frame: Up to 26, 52 and 104 weeks] [Designated as safety issue: No]

  COPD exacerbation is defined as any deterioration of symptoms that leads to an increase in bronchodilator use on 2 or more consecutive days, or administration (at investigator's discretion) of antibiotics and/or systemic corticosteroids (above participant's usual dose), or an unscheduled COPD-related doctor visit, hospitalization or emergency room treatment. The percentages of participants who experienced at least one moderate to severe COPD exacerbation during the first 26 weeks, the first 52 weeks and the first 104 weeks of treatment were to be summarized.

- Total Exacerbations of Chronic Pulmonary Disease Tool-Patient-Recorded Outcome (EXACT-PRO) Questionnaire Score [Time Frame: At 26, 52 and 104 weeks] [Designated as safety issue: No]

  The total score on the EXACT-PRO questionnaire is used to determine the frequency, severity, and duration of exacerbations of COPD. The 14-item EXACT-PRO questionnaire was to be completed by participants every evening to describe their experience of COPD during that day. Assessments were included for Breathlessness (5 items), Cough and Sputum (2 items), Chest Symptoms (3 items), and 4 additional items (Difficulty with Sputum, Tired or Weak, Sleep Disturbance, and Psychological State). Each item was measured on a 5- or 6-point scale. The total EXACT-PRO questionnaire score could range from 0 to 100, with a higher score indicating a more severe health state.

- Induced Sputum Absolute Neutrophil Counts [Time Frame: Baseline, Week 26, Week 52, Week 104] [Designated as safety issue: No]

  Induced sputum samples were to be obtained from participants via the nebulized method for analysis of absolute neutrophil counts at Week 26, Week 52 and Week 104. The reported Baseline least squares (LS) means and standard deviations (SDs) are pooled across all treatment groups. The rationale for the use of pooled Baseline LS mean and SD values is the assumption that the Baseline LS mean and SD values are similar across treatment groups. The reported post-Baseline SDs are pooled across all treatment groups. The rationale for the use of an analysis of variance (ANOVA) method using pooled SD values is the assumption that the SDs are similar across treatment groups.

- Change From Baseline in St. George's Respiratory Questionnaire for COPD Patients (SGRQ-C) Total Score [Time Frame: Baseline and Week 26, Week 52, Week 104] [Designated as safety issue: No]

  The SGRQ-C consists of 40 items aggregated into 3 component scores: Symptoms (frequency/severity), Activity (limited by breathlessness), Impacts (social functioning, psychological disturbances), and a Total score. Each response to a question is assigned a weight. Component scores are calculated by summing the weights from all positive items in that component, dividing by the sum of weights for all items in that component, and multiplying this number by 100. Component scores could range from 0-100, with a higher component score indicating greater disease burden. The Total score is calculated by summing the weights to all the positive responses in each component, dividing by the sum of

weights for all items in the questionnaire, and multiplying this number by 100. SGRQ-C Total scores could range from 0-100, with a higher SGRQ-C Total score indicating greater disease burden. Participants were to assess their COPD symptoms, activity and impact at Baseline, Week 26, Week 52, and Week 104.

- Change From Baseline in Distance Walked in 6 Minutes (6-Minute Walk Test) [Time Frame: Baseline and Week 26, Week 52, Week 104] [Designated as safety issue: No]

  The 6-minute walk test measures the distance participants can walk quickly on a flat, hard surface in 6 minutes. The 6-minute walk test was to be conducted at Baseline, Week 26, Week 52 and Week 104.

- Change From Baseline in Pre-bronchodilator FEV1 [Time Frame: Baseline and Week 26, Week 52, Week 104] [Designated as safety issue: No]

  FEV1, as measured in liters by spirometry, is the amount of air expired in 1 second. Pre-bronchodilator FEV1 was to be assessed immediately before bronchodilator administration at Baseline, Week 26, Week 52 and Week 104.

- Change From Baseline in Forced Expiratory Flow During the Middle Half of the Forced Vital Capacity (FEF25%-75%) Test [Time Frame: Baseline and Week 26, Week 52, Week 104] [Designated as safety issue: No]

  Mid-Breath Forced Expiratory Flow (FEF25%-75%), as measured in liters/minute by spirometry, is the rate at which participants breathe out air from 25 percent of their breath to 75 percent of their breath. FEF25%-75% was to be assessed at Baseline, Week 26, Week 52 and Week 104.

- Change From Baseline in Post-bronchodilator Forced Vital Capacity (FVC) [Time Frame: Baseline and Week 26, Week 52, Week 104] [Designated as safety issue: No]

  FVC, as measured in liters by spirometry, is the amount of air forcibly exhaled from the lungs after taking the deepest breath possible. Post-bronchodilator FVC was to be assessed 30 minutes after bronchodilator administration (4 puffs of albuterol/salbutamol or equivalent separated by 30-second intervals) at Baseline, Week 26, Week 52 and Week 104.

- Change From Baseline in Functional Residual Capacity (FRC) [Time Frame: Baseline and Week 26, Week 52, Week 104] [Designated as safety issue: No]

  FRC, as measured in liters by body plethysmography, is the volume of air present in the lungs at the end of passive expiration. FRC was to be assessed after post-bronchodilator spirometry tests were performed at Baseline, Week 26, Week 52 and Week 104.

- Change From Baseline in Total Lung Capacity (TLC) [Time Frame: Baseline and Week 26, Week 52, Week 104] [Designated as safety issue: No]

  TLC, as measured in liters by body plethysmography, is the most amount of air lungs can hold at the top of breathing in. TLC was to be assessed after post-bronchodilator spirometry tests were performed at Baseline, Week 26, Week 52 and Week 104.

- Change From Baseline in Inspiratory Capacity (IC) [Time Frame: Baseline and Week 26, Week 52, Week 104] [Designated as safety issue: No]

  IC, as measured in liters by body plethysmography, is the maximum amount of air inspired when taking a slow, full inspiration with no hesitation from a position of passive end-tidal expiration (i.e. FRC) to a position of maximal inspiration. IC was to be assessed after post-bronchodilator spirometry tests were performed at Baseline, Week 26, Week 52 and Week 104.

- Change From Baseline in Morning Peak Expiratory Flow (PEF) [Time Frame: Baseline and Week 26, Week 52, Week 104] [Designated as safety issue: No]

  PEF, as measured in liters/minute with a peak flow meter, is the maximum speed of expiration. Participants were to perform at least 3 and up to 5 PEF measurements in the morning before taking study drug. PEF was to be assessed at Baseline, Week 26, Week 52 and Week 104.

- Change From Baseline in Body-Mass Index, Airflow Obstruction, Dyspnea, and Exercise Capacity (BODE) Index Score [Time Frame: Baseline and Week 26, Week 52, Week 104] [Designated as safety issue: No]

  The BODE index is a composite score assessing COPD prognosis that consists of 4 variables that are individually scored: FEV1 percent predicted, 6-Minute Walk Test, Modified Medical Research Council (MMRC) dyspnea scale and body mass index (BMI). The FEV1 percent predicted was scored from ≥65% (0 points, less airway obstruction) to ≤35% (3 points, greater airway obstruction). The 6-Minute Walk Distance was scored from: ≥350 meters (0 points, good exercise capacity) to ≤149 meters (3 points, poor exercise capacity). The MMRC Dyspnea Scale was scored from: MMRC 0: Dyspneic on strenuous exercise (0 points) to MMRC 4: Cannot leave house; breathless on dressing/undressing (3 points). BMI was scored as: >21 (0 points) and ≤21 (1 point). Variable scores were summed to produce a BODE index score. BODE index scores could range from 0 to 10, with a higher score correlating with an increased risk of COPD mortality. BODE index scores were to be assessed at Baseline, Week 26, Week 52 and Week 104.

- Change From Baseline in Modified Medical Research Council (MMRC) Dyspnea Score [Time Frame: Baseline and Week 26, Week 52, Week 104] [Designated as safety issue: No]

  The MMRC dyspnea scale is used to assess participant breathlessness. The MMRC dyspnea scale consists of five grades that describe almost the entire range of respiratory disability from none (Grade 0=Not troubled with breathlessness except with strenuous exercise) to almost complete incapacity (Grade 4=Too breathless to leave the house or breathless when dressing or undressing). MMRC dyspnea scores were to be assessed at Baseline, Week 26, Week 52 and Week 104.

- Sputum Inflammatory Marker Levels: Interleukin 8 (IL-8) [Time Frame: Baseline, Week 26, Week 52, Week 104] [Designated as safety issue: No]

  Induced sputum samples were to be collected from participants via the nebulized method prior to study drug administration at Week 26, Week 52 and Week 104. IL-8 levels were measured by enzyme-linked immunosorbent assay (ELISA) in the sputum supernatant. The reported Baseline LS means and SDs are pooled across all treatment groups. The rationale for the use of pooled Baseline LS mean and SD values is the assumption that the Baseline LS mean and SD values are similar across treatment groups. The reported post-Baseline SDs are pooled across all treatment groups. The rationale for the use of an ANOVA method using pooled SD values is the assumption that the SDs are similar across treatment groups.

- Sputum Inflammatory Marker Levels: Myeloperoxidase (MPO) [Time Frame: Baseline, Week 26, Week 52, Week 104] [Designated as safety issue: No]

  Induced sputum samples were to be collected from participants via the nebulized method prior to study drug administration at Week 26, Week 52 and Week 104. MPO levels were measured by ELISA in the sputum supernatant. The reported Baseline LS means and SDs are pooled across all treatment groups. The rationale for the use of pooled Baseline LS mean and SD values is the assumption that the Baseline LS mean and SD values are similar across treatment groups. The reported post-Baseline SDs are pooled across all treatment groups. The rationale for the use of an ANOVA method using pooled SD values is the assumption that the SDs are similar across treatment groups.

- Sputum Inflammatory Marker Levels: Sputum Neutrophil Elastase [Time Frame: Baseline, Week 26, Week 52, Week 104] [Designated as safety issue: No]

  Induced sputum samples were to be collected from participants via the nebulized method prior to study drug administration at Week 26, Week 52 and Week 104. Neutrophil elastase levels were measured in the sputum supernatant. The reported Baseline LS means and SDs are pooled across all treatment groups. The rationale for the use of pooled Baseline LS mean and SD values is the assumption that the Baseline LS mean and SD values are similar across treatment groups. The reported post-Baseline SDs are pooled across all treatment groups. The rationale for the use of an ANOVA method using pooled SD values is the assumption that the SDs are similar across treatment groups.

- Sputum Inflammatory Marker Levels: Matrix Metallopeptidase-9 (MMP-9) [Time Frame: Baseline, Week 26, Week 52, Week 104] [Designated as safety issue: No]

  Induced sputum samples were to be collected from participants via the nebulized method prior to study drug administration at Week 26, Week 52 and Week 104. MMP-9 levels were measured by ELISA in the sputum supernatant. The reported Baseline LS means and SDs are pooled across all treatment groups. The rationale for the use of pooled Baseline LS mean and SD values is the assumption that the Baseline LS mean and SD values are similar across treatment groups. The reported post-Baseline SDs are pooled across all treatment groups. The rationale for the use of an ANOVA method using pooled SD values is the assumption that the SDs are similar across treatment groups.

- Plasma Inflammatory Biomarker Levels: High-sensitivity C-reactive Protein (Hs-CRP) [Time Frame: Baseline, Week 26, Week 52, Week 104] [Designated as safety issue: No]

  Blood samples were to be collected prior to study drug administration to determine participant plasma hs-CRP levels at Week 26, Week 52 and Week 104. The reported Baseline LS means and SDs are pooled across all treatment groups. The rationale for the use of pooled Baseline LS mean and SD values is the assumption that the Baseline LS mean and SD values are similar across treatment groups. The reported post-Baseline SDs are pooled across all treatment groups. The rationale for the use of an ANOVA method using pooled SD values is the assumption that the SDs are similar across treatment groups.

- Plasma Inflammatory Biomarker Levels: Fibrinogen [Time Frame: Baseline, Week 26, Week 52, Week 104] [Designated as safety issue: No]

  Blood samples were to be collected prior to study drug administration to determine participant plasma fibrinogen levels at Week 26, Week 52 and Week 104. The reported Baseline LS means and SDs are pooled across all treatment groups. The rationale for the use of pooled Baseline LS mean and SD values is the assumption that the Baseline LS mean and SD values are similar across treatment groups. The reported post-Baseline SDs are pooled across all treatment groups. The rationale for the use of an ANOVA method using pooled SD values is the assumption that the SDs are similar across treatment groups.

- Plasma Inflammatory Biomarker Levels: Myeloperoxidase (MPO) [Time Frame: Baseline, Week 26, Week 52, Week 104] [Designated as safety issue: No]

  Blood samples were to be collected prior to study drug administration to determine participant plasma MPO levels at Week 26, Week 52 and

Week 104. The reported Baseline LS means and SDs are pooled across all treatment groups. The rationale for the use of pooled Baseline LS mean and SD values is the assumption that the Baseline LS mean and SD values are similar across treatment groups. The reported post-Baseline SDs are pooled across all treatment groups. The rationale for the use of an ANOVA method using pooled SD values is the assumption that the SDs are similar across treatment groups.

- Plasma Inflammatory Biomarker Levels: Matrix Metallopeptidase-9 (MMP-9) [Time Frame: Baseline, Week 26, Week 52, Week 104] [Designated as safety issue: No]

  Blood samples were to be collected prior to study drug administration to determine participant plasma MMP-9 levels at Week 26, Week 52 and Week 104. The reported Baseline LS means and SDs are pooled across all treatment groups. The rationale for the use of pooled Baseline LS mean and SD values is the assumption that the Baseline LS mean and SD values are similar across treatment groups. The reported post-Baseline SDs are pooled across all treatment groups. The rationale for the use of an ANOVA method using pooled SD values is the assumption that the SDs are similar across treatment groups.

- Plasma Inflammatory Biomarker Levels: Plasma Neutrophil Elastase [Time Frame: Baseline, Week 26, Week 52, Week 104] [Designated as safety issue: No]

  Blood samples were to be collected prior to study drug administration to determine participant plasma neutrophil elastase levels at Week 26, Week 52 and Week 104. The reported Baseline LS means and SDs are pooled across all treatment groups. The rationale for the use of pooled Baseline LS mean and SD values is the assumption that the Baseline LS mean and SD values are similar across treatment groups. The reported post-Baseline SDs are pooled across all treatment groups. The rationale for the use of an ANOVA method using pooled SD values is the assumption that the SDs are similar across treatment groups.

- Plasma Inflammatory Biomarker Levels: Epithelial Cell-Derived Neutrophil Activating Peptide 78 (ENA-78) [Time Frame: Baseline, Week 26, Week 52, Week 104] [Designated as safety issue: No]

  Blood samples were to be collected prior to study drug administration to determine participant plasma ENA-78 levels at Week 26, Week 52 and Week 104. The reported Baseline LS means and SDs are pooled across all treatment groups. The rationale for the use of pooled Baseline LS mean and SD values is the assumption that the Baseline LS mean and SD values are similar across treatment groups. The reported post-Baseline SDs are pooled across all treatment groups. The rationale for the use of an ANOVA method using pooled SD values is the assumption that the SDs are similar across treatment groups.

- Change From Baseline in Pre- and Post-6-Minute-Walk-Test Borg Scale Score [Time Frame: Baseline and Week 26, Week 52, Week 104] [Designated as safety issue: No]

  The 6-minute walk test measured the distance participants could walk quickly on a flat, hard surface in 6 minutes. The Borg scale is a method use to rate perceived exertion (0=Nothing at all [no exertion] to 10=Maximal [exertion]). Borg scale scores were to be assessed pre- and post-walk-test at Baseline, Week 26, Week 52 and Week 104. A higher score indicates greater perceived exertion.

- Change From Baseline in Percent of Arterial Oxygen Saturation Measured by Pulse Oximetry Before and After the 6-Minute Walk Test [Time Frame: Baseline and Week 26, Week 52, Week 104] [Designated as safety issue: No]

  The 6-minute walk test measured the distance participants could walk quickly on a flat, hard surface in 6 minutes. Percent (%) of arterial oxygen saturation, as measured by pulse oximetry, was to be assessed before and after the 6-minute walk test at Baseline, Week 26, Week 52 and Week 104.

- Percentage of Participants Who Experienced an AE Related to Respiratory Infection [Time Frame: Up to 26 , 52 and 104 weeks] [Designated as safety issue: Yes]

  The percentage of participants who experienced an AE related to a respiratory infection or infestation, was to be calculated for the first 26 weeks, the first 52 weeks and the first 104 weeks of treatment.

- Percentage of Participants Who Experienced an AE Related to Any Type of Infection [Time Frame: Up to 26 , 52 and 104 weeks] [Designated as safety issue: Yes]

  The percentage of participants who experienced an AE related to any type of infection or infestation, was to be calculated for the first 26 weeks, the first 52 weeks and the first 104 weeks of treatment.

Enrollment:	616
Study Start Date:	October 2009
Study Completion Date:	November 2011
Primary Completion Date:	March 2011 (Final data collection date for primary outcome measure)

Arms	Assigned Interventions

Experimental: Navarixin 10 mg Participants receive navarixin 10 mg, as one navarixin 10 mg capsule and two placebo capsules, administered orally once daily (QD) for up to 2 years	Drug: Navarixin Navarixin 10 mg and 30 mg capsules Drug: Placebo Placebo to navarixin capsules Drug: Rescue medication Short-acting β-agonist (SABA), anticholinergic, or a combination SABA/anticholinergic
Experimental: Navarixin 30 mg Participants receive navarixin 30 mg, as one navarixin 30 mg capsule and two placebo capsules, administered orally QD for up to 2 years	Drug: Navarixin Navarixin 10 mg and 30 mg capsules Drug: Placebo Placebo to navarixin capsules Drug: Rescue medication Short-acting β-agonist (SABA), anticholinergic, or a combination SABA/anticholinergic
Experimental: Navarixin 50 mg Participants receive navarixin 50 mg, as two navarixin 10 mg capsules and one navarixin 30 mg capsule, administered orally QD for up to 2 years	Drug: Navarixin Navarixin 10 mg and 30 mg capsules Drug: Rescue medication Short-acting β-agonist (SABA), anticholinergic, or a combination SABA/anticholinergic
Placebo Comparator: Placebo Participants receive placebo to navarixin, as three placebo capsules, administered orally QD for up to 2 years	Drug: Placebo Placebo to navarixin capsules Drug: Rescue medication Short-acting β-agonist (SABA), anticholinergic, or a combination SABA/anticholinergic

Eligibility

Ages Eligible for Study: 41 Years to 75 Years
Genders Eligible for Study: Both
Accepts Healthy Volunteers: No

Criteria

Inclusion Criteria:

- Diagnosis of COPD for at least 2 years based on American Thoracic Society/European Respiratory Society (ATS/ERS) current guidelines or symptoms consistent with COPD for at least 2 years.
- >40 to <=75 years of age, of either sex, and of any race.
- No exacerbation or respiratory infection in the past 6 weeks.
- Smoker or ex-smoker with more than 10 pack-year history.

Exclusion Criteria:

- Diagnosis of asthma or other clinically relevant lung disease (other than COPD), i.e., sarcoidosis, tuberculosis, pulmonary fibrosis, severe bronchiectasis, or lung cancer.
- Significant X-ray findings.
- Use of supplemental oxygen for >12 hours/day.

Contacts and Locations

Choosing to participate in a study is an important personal decision. Talk with your doctor and family members or friends about deciding to join a study. To learn more about this study, you or your doctor may contact the study research staff using the Contacts provided below. For general information, see Learn About Clinical Studies.

Please refer to this study by its ClinicalTrials.gov identifier: NCT01006616

Sponsors and Collaborators

Merck Sharp & Dohme Corp.

Investigators

Study Director: Medical Director Merck Sharp & Dohme Corp.

More Information

Publications:

Rennard SI, Dale DC, Donohue JF, Kanniess F, Magnussen H, Sutherland ER, Watz H, Lu S, Stryszak P, Rosenberg E, Staudinger H. CXCR2 Antagonist MK-7123. A Phase 2 Proof-of-Concept Trial for Chronic Obstructive Pulmonary Disease. Am J Respir Crit Care Med. 2015 May 1;191(9):1001-11. doi: 10.1164/rccm.201405-0992OC.

Responsible Party:	Merck Sharp & Dohme Corp.
ClinicalTrials.gov Identifier:	NCT01006616 History of Changes
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Study First Received:	October 1, 2009
Results First Received:	October 2, 2014
Last Updated:	April 24, 2015
Health Authority:	Canada: Health Canada

ClinicalTrials.gov processed this record on May 08, 2016

TO TOP

For Patients and Families | For Researchers | For Study Record Managers

HOME RSS FEEDS SITE MAP TERMS AND CONDITIONS DISCLAIMER CONTACT NLM HELP DESK

Long-Term Study of the Effects of Navarixin (SCH 527123, MK-7123) in Participants With Moderate to Severe COPD (MK-7123-019)

This study has been terminated.

Sponsor:
Merck Sharp & Dohme Corp.

Information provided by (Responsible Party):
Merck Sharp & Dohme Corp.

ClinicalTrials.gov Identifier:
NCT01006616

First received: October 1, 2009
Last updated: April 24, 2015
Last verified: April 2015
History of Changes

Results First Received: October 2, 2014

Study Type:	Interventional
Study Design:	Allocation: Randomized; Endpoint Classification: Efficacy Study; Intervention Model: Parallel Assignment; Masking: Double Blind (Subject, Investigator); Primary Purpose: Treatment
Condition:	COPD
Interventions:	Drug: Navarixin Drug: Placebo Drug: Rescue medication

Participant Flow

Hide Participant Flow

Recruitment Details

Key information relevant to the recruitment process for the overall study, such as dates of the recruitment period and locations
No text entered.

Pre-Assignment Details

Significant events and approaches for the overall study following participant enrollment, but prior to group assignment
No text entered.

Reporting Groups

	Description
Navarixin 10 mg	Participants receive navarixin 10 mg, as one navarixin 10 mg capsule and two placebo capsules, administered orally once daily (QD) for up to 2 years
Navarixin 30 mg	Participants receive navarixin 30 mg, as one navarixin 30 mg capsule and two placebo capsules, administered orally QD for up to 2 years
Navarixin 50 mg	Participants receive navarixin 50 mg, as two navarixin 10 mg capsules and one navarixin 30 mg capsule, administered orally QD for up to 2 years
Placebo	Participants receive placebo to navarixin, as three placebo capsules, administered orally QD for up to 2 years

Participant Flow for 2 periods

Period 1: Period 1 (6 Months)

	Navarixin 10 mg	Navarixin 30 mg	Navarixin 50 mg	Placebo
STARTED	152	156	153	155
Treated	152	156	152	154
COMPLETED	126	102	102	128
NOT COMPLETED	26	54	51	27
Adverse Event	10	31	37	9
Lack of Efficacy	3	4	0	4
Lost to Follow-up	0	0	1	0
Withdrew, Reason Unrelated to Treatment	6	5	2	3
Withdrew, Reason Related to Treatment	0	3	1	2
Withdrawal by Subject	2	2	2	0
Did Not Meet Protocol Eligibility	5	7	5	5
Noncompliance With Protocol	0	2	2	3
Not Treated	0	0	1	1

Period 2: Period 2 (18 Months)

	Navarixin 10 mg	Navarixin 30 mg	Navarixin 50 mg	Placebo
STARTED	75 [1]	63 [1]	55 [1]	82 [1]
Treated	75	63	55	82
COMPLETED	0	0	0	0
NOT COMPLETED	75	63	55	82
Adverse Event	6	6	6	4

Lack of Efficacy	**0**	**0**	**1**	**2**
Lost to Follow-up	**2**	**0**	**0**	**0**
Withdrew, Reason Unrelated to Treatment	**3**	**0**	**3**	**2**
Withdrew, Reason Related to Treatment	**0**	**6**	**1**	**2**
Withdrawal by Subject	**1**	**4**	**0**	**1**
Noncompliance With Protocol	**0**	**1**	**0**	**1**
Study Terminated	**63**	**46**	**44**	**70**

[1] Period 2 was optional. Not all participants completing Period 1 continued into Period 2.

Baseline Characteristics

Hide Baseline Characteristics

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Baseline Analysis Population consists of all treated participants (1 participant in the Navarixin 50 mg group and 1 participant in the Placebo group did not receive study drug).

Reporting Groups

	Description
Navarixin 10 mg	Participants receive navarixin 10 mg, as one navarixin 10 mg capsule and two placebo capsules, administered orally QD for up to 2 years
Navarixin 30 mg	Participants receive navarixin 30 mg, as one navarixin 30 mg capsule and two placebo capsules, administered orally QD for up to 2 years
Navarixin 50 mg	Participants receive navarixin 50 mg, as two navarixin 10 mg capsules and one navarixin 30 mg capsule, administered orally QD for up to 2 years
Placebo	Participants receive placebo to navarixin, as three placebo capsules, administered orally QD for up to 2 years
Total	Total of all reporting groups

Baseline Measures

	Navarixin 10 mg	**Navarixin 30 mg**	**Navarixin 50 mg**	**Placebo**	**Total**
Number of Participants [units: participants]	**152**	**156**	**152**	**154**	**614**
Age [units: Years] Mean (Standard Deviation)	**63.7 (6.9)**	**63.2 (7.4)**	**61.3 (7.5)**	**63.3 (7.2)**	**62.9 (7.3)**
Gender [units: Participants]					
Female	**28**	**52**	**50**	**46**	**176**
Male	**124**	**104**	**102**	**108**	**438**

Outcome Measures

Hide All Outcome Measures

1. Primary: Change From Baseline in Post-bronchodilator Forced Expiratory Volume in 1 Second (FEV1) (Period 1) [Time Frame: Baseline and Week 26]

Measure Type	Primary
Measure Title	Change From Baseline in Post-bronchodilator Forced Expiratory Volume in 1 Second (FEV1) (Period 1)
Measure Description	FEV1, as measured in liters by spirometry, is the amount of air expired in 1 second. Participants were assessed for post-bronchodilator FEV1 30 minutes after bronchodilator administration (4 puffs of albuterol/salbutamol or equivalent separated by 30-second intervals) (reversibility test) at Baseline and Week 26.
Time Frame	Baseline and Week 26
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The Full Analysis Set (FAS) population consisted of all participants who received at least one dose of study drug and had a Baseline and Week 26 assessment for post-bronchodilator FEV1.

Reporting Groups

	Description
Navarixin 10 mg	Participants receive navarixin 10 mg, as one navarixin 10 mg capsule and two placebo capsules, administered orally QD for up to 2 years
Navarixin 30 mg	Participants receive navarixin 30 mg, as one navarixin 30 mg capsule and two placebo capsules, administered orally QD for up to 2 years
Navarixin 50 mg	Participants receive navarixin 50 mg, as two navarixin 10 mg capsules and one navarixin 30 mg capsule, administered orally QD for up to 2 years
Placebo	Participants receive placebo to navarixin, as three placebo capsules, administered orally QD for up to 2 years

Measured Values

	Navarixin 10 mg	**Navarixin 30 mg**	**Navarixin 50 mg**	**Placebo**
Number of Participants Analyzed [units: participants]	**124**	**105**	**102**	**127**
Change From Baseline in Post-bronchodilator Forced Expiratory Volume in 1 Second (FEV1) (Period 1) [units: Liters] Least Squares Mean (Standard Error)	**-0.009 (0.022)**	**-0.068 (0.023)**	**0.028 (0.024)**	**-0.039 (0.022)**

Statistical Analysis 1 for Change From Baseline in Post-bronchodilator Forced Expiratory Volume in 1 Second (FEV1) (Period 1)

Groups [1]	Navarixin 10 mg vs. Placebo
Method [2]	Constrained Longitudinal Data Analysis
P Value [3]	0.325
Mean Difference (Net) [4]	0.031

95% Confidence Interval	-0.030 to 0.091

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	Model with treatment, time, treatment by time interaction, and baseline smoking status (yes/no) and inhaled corticosteroid (ICS) use (yes/no)
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

Statistical Analysis 2 for Change From Baseline in Post-bronchodilator Forced Expiratory Volume in 1 Second (FEV1) (Period 1)

Groups [1]	Navarixin 30 mg vs. Placebo
Method [2]	Constrained Longitudinal Data Analysis
P Value [3]	0.370
Mean Difference (Net) [4]	-0.029
95% Confidence Interval	-0.091 to 0.034

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	Model with treatment, time, treatment by time interaction, and baseline smoking status (yes/no) and ICS use (yes/no)
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

Statistical Analysis 3 for Change From Baseline in Post-bronchodilator Forced Expiratory Volume in 1 Second (FEV1) (Period 1)

Groups [1]	Navarixin 50 mg vs. Placebo
Method [2]	Constrained Longitudinal Data Analysis
P Value [3]	0.037
Mean Difference (Net) [4]	0.067
95% Confidence Interval	0.004 to 0.131

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:

	Model with treatment, time, treatment by time interaction, and baseline smoking status (yes/no) and ICS use (yes/no)
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

2. Primary: Percentage of Participants With an Adverse Event (AE) Related to a Blood Absolute Neutrophil Count (ANC) of Less Than 1.5x10^9 Cells/L [Time Frame: Up to 104 weeks]

Measure Type	Primary
Measure Title	Percentage of Participants With an Adverse Event (AE) Related to a Blood Absolute Neutrophil Count (ANC) of Less Than 1.5x10^9 Cells/L
Measure Description	The percentage of participants who experienced an AE related to an ANC of less than 1.5x10^9 cells/L at one or more visits during the first 26 weeks, the first 52 weeks and the first 104 weeks was to be calculated.
Time Frame	Up to 104 weeks
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The All Subjects as Treated (ASaT) population consisted of all participants who received at least one dose of study drug. The study was terminated during Period 2; no data were analyzed for this endpoint for up to 52 and up to 104 weeks.

Reporting Groups

	Description
Navarixin 10 mg	Participants receive navarixin 10 mg, as one navarixin 10 mg capsule and two placebo capsules, administered orally QD for up to 2 years
Navarixin 30 mg	Participants receive navarixin 30 mg, as one navarixin 30 mg capsule and two placebo capsules, administered orally QD for up to 2 years
Navarixin 50 mg	Participants receive navarixin 50 mg, as two navarixin 10 mg capsules and one navarixin 30 mg capsule, administered orally QD for up to 2 years
Placebo	Participants receive placebo to navarixin, as three placebo capsules, administered orally QD for up to 2 years

Measured Values

	Navarixin 10 mg	**Navarixin 30 mg**	**Navarixin 50 mg**	**Placebo**
Number of Participants Analyzed [units: participants]	**152**	**156**	**152**	**154**
Percentage of Participants With an Adverse Event (AE) Related to a Blood Absolute Neutrophil Count (ANC) of Less Than 1.5x10^9 Cells/L [units: Percentage of Participants]				
Up to Week 26 (n=152, 156, 152,154)	**3.3**	**12.8**	**20.4**	**0.6**
Up to Week 52 (n=0, 0, 0, 0)	**[1]**	**[1]**	**[1]**	**[1]**

	NA	NA	NA	NA
Up to Week 104 (n=0, 0, 0, 0)	NA [1]	NA [1]	NA [1]	NA [1]

[1] Study terminated; data not collected.

Statistical Analysis 1 for Percentage of Participants With an Adverse Event (AE) Related to a Blood Absolute Neutrophil Count (ANC) of Less Than 1.5x10^9 Cells/L

Groups [1]	Navarixin 10 mg vs. Placebo
Method [2]	Miettinen and Nurminen
P Value [3]	0.096
Difference in percentages [4]	2.6
95% Confidence Interval	-0.6 to 6.9

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	Analysis of Week 26 data

Statistical Analysis 2 for Percentage of Participants With an Adverse Event (AE) Related to a Blood Absolute Neutrophil Count (ANC) of Less Than 1.5x10^9 Cells/L

Groups [1]	Navarixin 30 mg vs. Placebo
Method [2]	Miettinen and Nurminen
P Value [3]	<0.001
Difference in percentages [4]	12.2
95% Confidence Interval	7.4 to 18.4

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	Analysis of Week 26 data

Statistical Analysis 3 for Percentage of Participants With an Adverse Event (AE) Related to a Blood Absolute Neutrophil Count (ANC) of Less Than 1.5x10^9 Cells/L

Groups [1]	Navarixin 50 mg vs. Placebo
Method [2]	Miettinen and Nurminen
P Value [3]	<0.001
Difference in percentages [4]	19.7
95% Confidence Interval	13.8 to 26.9

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	Analysis of Week 26 data

3. Secondary: Change From Baseline in Post-bronchodilator FEV1 (Period 2) [Time Frame: Baseline and Week 52, Week 104]

Measure Type	Secondary
Measure Title	Change From Baseline in Post-bronchodilator FEV1 (Period 2)
Measure Description	FEV1, as measured in liters by spirometry, is the amount of air expired in 1 second. Participants were to be assessed for post-bronchodilator FEV1 30 minutes after bronchodilator administration (4 puffs of albuterol/salbutamol or equivalent separated by 30-second intervals) (reversibility test) at Baseline, Week 52 and Week 104.
Time Frame	Baseline and Week 52, Week 104
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The FAS population consisted of all participants who received at least one dose of study drug and had a Baseline and Week 52 or Week 104 assessment for post-bronchodilator FEV1 in Period 2. The study was terminated during Period 2; no data were collected for this endpoint at Week 104.

Reporting Groups

	Description
Navarixin 10 mg	Participants receive navarixin 10 mg, as one navarixin 10 mg capsule and two placebo capsules, administered orally QD for up to 2 years
Navarixin 30 mg	Participants receive navarixin 30 mg, as one navarixin 30 mg capsule and two placebo capsules, administered orally QD for up to 2 years
Navarixin 50 mg	Participants receive navarixin 50 mg, as two navarixin 10 mg capsules and one navarixin 30 mg capsule, administered orally

	QD for up to 2 years
Placebo	Participants receive placebo to navarixin, as three placebo capsules, administered orally QD for up to 2 years

Measured Values

	Navarixin 10 mg	Navarixin 30 mg	Navarixin 50 mg	Placebo
Number of Participants Analyzed [units: participants]	**66**	**47**	**44**	**65**
Change From Baseline in Post-bronchodilator FEV1 (Period 2) [units: Liters] Least Squares Mean (Standard Error)				
Week 52 (n=66, 47, 44, 65)	**-0.047 (0.027)**	**-0.084 (0.031)**	**0.028 (0.032)**	**-0.031 (0.027)**
Week 104 (n=0, 0, 0, 0)	**NA [1]**	**NA [1]**	**NA [1]**	**NA [1]**

[1] Study terminated; data not collected.

No statistical analysis provided for Change From Baseline in Post-bronchodilator FEV1 (Period 2)

4. Secondary: Number of Participants With a Moderate to Severe Chronic Obstructive Pulmonary Disease (COPD) Exacerbation [Time Frame: Up to 26 , 52 and 104 weeks]

Measure Type	Secondary
Measure Title	Number of Participants With a Moderate to Severe Chronic Obstructive Pulmonary Disease (COPD) Exacerbation
Measure Description	COPD exacerbation is defined as any deterioration of symptoms that leads to an increase in bronchodilator use on 2 or more consecutive days, or administration (at investigator's discretion) of antibiotics and/or systemic corticosteroids (above participant's usual dose), or an unscheduled COPD-related doctor visit, hospitalization or emergency room treatment. The numbers of participants who experienced at least one moderate to severe COPD exacerbation during the first 26 weeks, the first 52 weeks and the first 104 weeks of treatment were to be summarized.
Time Frame	Up to 26 , 52 and 104 weeks
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The FAS population consisted of all participants who received at least one dose of study drug and had a Week 26, Week 52 or Week 104 assessment for COPD exacerbation. The study was terminated during Period 2; no data were collected for this endpoint for up to 104 weeks.

Reporting Groups

	Description
Navarixin 10 mg	Participants receive navarixin 10 mg, as one navarixin 10 mg capsule and two placebo capsules, administered orally QD for up to 2 years
Navarixin 30 mg	Participants receive navarixin 30 mg, as one navarixin 30 mg capsule and two placebo capsules, administered orally QD for up to 2 years
Navarixin 50 mg	Participants receive navarixin 50 mg, as two navarixin 10 mg capsules and one navarixin 30 mg capsule, administered orally QD for up to 2 years

Placebo	Participants receive placebo to navarixin, as three placebo capsules, administered orally QD for up to 2 years

Measured Values

	Navarixin 10 mg	Navarixin 30 mg	Navarixin 50 mg	Placebo
Number of Participants Analyzed [units: participants]	**152**	**156**	**152**	**154**
Number of Participants With a Moderate to Severe Chronic Obstructive Pulmonary Disease (COPD) Exacerbation [units: Participants]				
Up to Week 26 (n=152, 156, 152, 154)	**40**	**50**	**45**	**48**
Up to Week 52 (n=152, 156, 152, 154)	**50**	**58**	**51**	**53**
Up to Week 104 (n=0, 0, 0, 0)	**NA [1]**	**NA [1]**	**NA [1]**	**NA [1]**

[1] Study terminated; data not collected.

No statistical analysis provided for Number of Participants With a Moderate to Severe Chronic Obstructive Pulmonary Disease (COPD) Exacerbation

5. Secondary: Percentage of Participants With a Moderate to Severe COPD Exacerbation [Time Frame: Up to 26, 52 and 104 weeks]

Measure Type	Secondary
Measure Title	Percentage of Participants With a Moderate to Severe COPD Exacerbation
Measure Description	COPD exacerbation is defined as any deterioration of symptoms that leads to an increase in bronchodilator use on 2 or more consecutive days, or administration (at investigator's discretion) of antibiotics and/or systemic corticosteroids (above participant's usual dose), or an unscheduled COPD-related doctor visit, hospitalization or emergency room treatment. The percentages of participants who experienced at least one moderate to severe COPD exacerbation during the first 26 weeks, the first 52 weeks and the first 104 weeks of treatment were to be summarized.
Time Frame	Up to 26, 52 and 104 weeks
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The FAS population consisted of all participants who received at least one dose of study drug and had a Baseline and Week 26, Week 52 or Week 104 assessment for COPD exacerbation. The study was terminated during Period 2; no data were collected for this endpoint for up to 104 weeks.

Reporting Groups

	Description
Navarixin 10 mg	Participants receive navarixin 10 mg, as one navarixin 10 mg capsule and two placebo capsules, administered orally QD for up to 2 years
Navarixin 30 mg	Participants receive navarixin 30 mg, as one navarixin 30 mg capsule and two placebo capsules, administered orally QD for up to 2 years
Navarixin 50 mg	Participants receive navarixin 50 mg, as two navarixin 10 mg capsules and one navarixin 30 mg capsule, administered orally QD for up to 2 years

Placebo	Participants receive placebo to navarixin, as three placebo capsules, administered orally QD for up to 2 years

Measured Values

	Navarixin 10 mg	Navarixin 30 mg	Navarixin 50 mg	Placebo
Number of Participants Analyzed [units: participants]	**152**	**156**	**152**	**154**
Percentage of Participants With a Moderate to Severe COPD Exacerbation [units: Percentage of Participants]				
Up to Week 26 (n=152, 156, 152, 154)	**26.3**	**32.1**	**29.6**	**31.2**
Up to Week 52 (n=152, 156, 152, 154)	**32.9**	**37.2**	**33.6**	**34.4**
Up to Week 104 (n=0, 0, 0, 0)	**NA [1]**	**NA [1]**	**NA [1]**	**NA [1]**

[1] Study terminated; data not collected.

No statistical analysis provided for Percentage of Participants With a Moderate to Severe COPD Exacerbation

6. Secondary: Total Exacerbations of Chronic Pulmonary Disease Tool-Patient-Recorded Outcome (EXACT-PRO) Questionnaire Score [Time Frame: At 26, 52 and 104 weeks]

Measure Type	Secondary
Measure Title	Total Exacerbations of Chronic Pulmonary Disease Tool-Patient-Recorded Outcome (EXACT-PRO) Questionnaire Score
Measure Description	The total score on the EXACT-PRO questionnaire is used to determine the frequency, severity, and duration of exacerbations of COPD. The 14-item EXACT-PRO questionnaire was to be completed by participants every evening to describe their experience of COPD during that day. Assessments were included for Breathlessness (5 items), Cough and Sputum (2 items), Chest Symptoms (3 items), and 4 additional items (Difficulty with Sputum, Tired or Weak, Sleep Disturbance, and Psychological State). Each item was measured on a 5- or 6-point scale. The total EXACT-PRO questionnaire score could range from 0 to 100, with a higher score indicating a more severe health state.
Time Frame	At 26, 52 and 104 weeks
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The FAS population was to consist of all participants who received at least one dose of study drug and had a Baseline and Week 26, Week 52 or Week 104 assessment for total EXACT-PRO score. This analysis was not conducted if results for percentage of participants with moderate to severe COPD exacerbation suggested no need for further investigation.

Reporting Groups

	Description
Navarixin 10 mg	Participants receive navarixin 10 mg, as one navarixin 10 mg capsule and two placebo capsules, administered orally QD for up to 2 years
Navarixin 30 mg	Participants receive navarixin 30 mg, as one navarixin 30 mg capsule and two placebo capsules, administered orally QD for up to 2 years
Navarixin 50 mg	Participants receive navarixin 50 mg, as two navarixin 10 mg capsules and one navarixin 30 mg capsule, administered orally

	QD for up to 2 years
Placebo	Participants receive placebo to navarixin, as three placebo capsules, administered orally QD for up to 2 years

Measured Values

	Navarixin 10 mg	Navarixin 30 mg	Navarixin 50 mg	Placebo
Number of Participants Analyzed [units: participants]	**0**	**0**	**0**	**0**
Total Exacerbations of Chronic Pulmonary Disease Tool-Patient-Recorded Outcome (EXACT-PRO) Questionnaire Score				

No statistical analysis provided for Total Exacerbations of Chronic Pulmonary Disease Tool-Patient-Recorded Outcome (EXACT-PRO) Questionnaire Score

7. Secondary: Induced Sputum Absolute Neutrophil Counts [Time Frame: Baseline, Week 26, Week 52, Week 104]

Measure Type	Secondary
Measure Title	Induced Sputum Absolute Neutrophil Counts
Measure Description	Induced sputum samples were to be obtained from participants via the nebulized method for analysis of absolute neutrophil counts at Week 26, Week 52 and Week 104. The reported Baseline least squares (LS) means and standard deviations (SDs) are pooled across all treatment groups. The rationale for the use of pooled Baseline LS mean and SD values is the assumption that the Baseline LS mean and SD values are similar across treatment groups. The reported post-Baseline SDs are pooled across all treatment groups. The rationale for the use of an analysis of variance (ANOVA) method using pooled SD values is the assumption that the SDs are similar across treatment groups.
Time Frame	Baseline, Week 26, Week 52, Week 104
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The FAS population consisted of all participants at selected sites who received at least one dose of study drug and had a baseline and Week 26, Week 52 or Week 104 assessment for sputum neutrophil count. The study was terminated during Period 2; no data were collected for this endpoint at Week 104.

Reporting Groups

	Description
Navarixin 10 mg	Participants receive navarixin 10 mg, as one navarixin 10 mg capsule and two placebo capsules, administered orally QD for up to 2 years
Navarixin 30 mg	Participants receive navarixin 30 mg, as one navarixin 30 mg capsule and two placebo capsules, administered orally QD for up to 2 years
Navarixin 50 mg	Participants receive navarixin 50 mg, as two navarixin 10 mg capsules and one navarixin 30 mg capsule, administered orally QD for up to 2 years
Placebo	Participants receive placebo to navarixin, as three placebo capsules, administered orally QD for up to 2 years

Measured Values

	Navarixin 10 mg	Navarixin 30 mg	Navarixin 50 mg	

				Placebo
Number of Participants Analyzed [units: participants]	**30**	**29**	**33**	**33**
Induced Sputum Absolute Neutrophil Counts [units: 10^9 cells/L] Least Squares Mean (Standard Deviation)				
Baseline (n=30, 29, 33, 33)	**1.485 (0.706)**	**1.485 (0.706)**	**1.485 (0.706)**	**1.485 (0.706)**
Week 26 (n=23, 13, 13, 17)	**1.763 (0.736)**	**2.073 (0.736)**	**0.860 (0.736)**	**2.121 (0.736)**
Week 52 (n=9, 8, 3, 3)	**2.884 (0.462)**	**2.022 (0.462)**	**1.253 (0.462)**	**3.218 (0.462)**
Week 104 (n=0, 0, 0, 0)	**NA [1]**	**NA [1]**	**NA [1]**	**NA [1]**

[1] Study terminated; data not collected.

No statistical analysis provided for Induced Sputum Absolute Neutrophil Counts

8. Secondary: Change From Baseline in St. George's Respiratory Questionnaire for COPD Patients (SGRQ-C) Total Score [Time Frame: Baseline and Week 26, Week 52, Week 104]

Measure Type	Secondary
Measure Title	Change From Baseline in St. George's Respiratory Questionnaire for COPD Patients (SGRQ-C) Total Score
Measure Description	The SGRQ-C consists of 40 items aggregated into 3 component scores: Symptoms (frequency/severity), Activity (limited by breathlessness), Impacts (social functioning, psychological disturbances), and a Total score. Each response to a question is assigned a weight. Component scores are calculated by summing the weights from all positive items in that component, dividing by the sum of weights for all items in that component, and multiplying this number by 100. Component scores could range from 0-100, with a higher component score indicating greater disease burden. The Total score is calculated by summing the weights to all the positive responses in each component, dividing by the sum of weights for all items in the questionnaire, and multiplying this number by 100. SGRQ-C Total scores could range from 0-100, with a higher SGRQ-C Total score indicating greater disease burden. Participants were to assess their COPD symptoms, activity and impact at Baseline, Week 26, Week 52, and Week 104.
Time Frame	Baseline and Week 26, Week 52, Week 104
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The FAS population consisted of all participants who received at least one dose of study drug and had a Baseline and Week 26, Week 52 or Week 104 assessment for SGRQ-C score. The study was terminated during Period 2; no data were collected for this endpoint at Week 104.

Reporting Groups

	Description
Navarixin 10 mg	Participants receive navarixin 10 mg, as one navarixin 10 mg capsule and two placebo capsules, administered orally QD for up to 2 years
Navarixin 30 mg	Participants receive navarixin 30 mg, as one navarixin 30 mg capsule and two placebo capsules, administered orally QD for up to 2 years

Navarixin 50 mg	Participants receive navarixin 50 mg, as two navarixin 10 mg capsules and one navarixin 30 mg capsule, administered orally QD for up to 2 years
Placebo	Participants receive placebo to navarixin, as three placebo capsules, administered orally QD for up to 2 years

Measured Values

	Navarixin 10 mg	Navarixin 30 mg	Navarixin 50 mg	Placebo
Number of Participants Analyzed [units: participants]	**130**	**112**	**106**	**131**
Change From Baseline in St. George's Respiratory Questionnaire for COPD Patients (SGRQ-C) Total Score [units: Score on a Scale] Least Squares Mean (Standard Error)				
Change at Week 26 (n=130, 112, 106, 131)	**-2.65 (1.15)**	**-2.28 (1.21)**	**-4.63 (1.23)**	**-1.60 (1.15)**
Change at Week 52 (n=62, 50, 45, 63)	**-2.49 (1.58)**	**-2.22 (1.73)**	**-3.86 (1.80)**	**-4.40 (1.57)**
Change at Week 104 (n=0, 0, 0, 0)	**NA [1]**	**NA [1]**	**NA [1]**	**NA [1]**

[1] Study terminated; data not collected.

No statistical analysis provided for Change From Baseline in St. George's Respiratory Questionnaire for COPD Patients (SGRQ-C) Total Score

9. Secondary: Change From Baseline in Distance Walked in 6 Minutes (6-Minute Walk Test) [Time Frame: Baseline and Week 26, Week 52, Week 104]

Measure Type	Secondary
Measure Title	Change From Baseline in Distance Walked in 6 Minutes (6-Minute Walk Test)
Measure Description	The 6-minute walk test measures the distance participants can walk quickly on a flat, hard surface in 6 minutes. The 6-minute walk test was to be conducted at Baseline, Week 26, Week 52 and Week 104.
Time Frame	Baseline and Week 26, Week 52, Week 104
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The FAS population consisted of all participants at selected sites who received at least one dose of study drug and had a Baseline and Week 26, Week 52 or Week 104 assessment for 6-minute walk test. The study was terminated during Period 2; no data were collected for this endpoint at Week 104.

Reporting Groups

	Description
Navarixin 10 mg	Participants receive navarixin 10 mg, as one navarixin 10 mg capsule and two placebo capsules, administered orally QD for up to 2 years
Navarixin 30 mg	Participants receive navarixin 30 mg, as one navarixin 30 mg capsule and two placebo capsules, administered orally QD for up to 2 years
Navarixin 50 mg	Participants receive navarixin 50 mg, as two navarixin 10 mg capsules and one navarixin 30 mg capsule, administered orally

	QD for up to 2 years
Placebo	Participants receive placebo to navarixin, as three placebo capsules, administered orally QD for up to 2 years

Measured Values

	Navarixin 10 mg	Navarixin 30 mg	Navarixin 50 mg	Placebo
Number of Participants Analyzed [units: participants]	**84**	**77**	**68**	**87**
Change From Baseline in Distance Walked in 6 Minutes (6-Minute Walk Test) [units: Meters] Least Squares Mean (Standard Error)				
Change at Week 26 (n=84, 77, 68, 87)	**18.87 (6.55)**	**-1.04 (6.79)**	**2.06 (7.19)**	**7.41 (6.45)**
Change at Week 52 (n=32, 25, 25, 30)	**19.79 (11.50)**	**-33.58 (12.74)**	**0.93 (12.84)**	**-15.37 (11.77)**
Change at Week 104 (n=0, 0, 0, 0)	**NA [1]**	**NA [1]**	**NA [1]**	**NA [1]**

[1] Study terminated; data not collected.

No statistical analysis provided for Change From Baseline in Distance Walked in 6 Minutes (6-Minute Walk Test)

10. Secondary: Change From Baseline in Pre-bronchodilator FEV1 [Time Frame: Baseline and Week 26, Week 52, Week 104]

Measure Type	Secondary
Measure Title	Change From Baseline in Pre-bronchodilator FEV1
Measure Description	FEV1, as measured in liters by spirometry, is the amount of air expired in 1 second. Pre-bronchodilator FEV1 was to be assessed immediately before bronchodilator administration at Baseline, Week 26, Week 52 and Week 104.
Time Frame	Baseline and Week 26, Week 52, Week 104
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The FAS population consisted of all participants who received at least one dose of study drug and had a Baseline and Week 26, Week 52 or Week 104 assessment for pre-bronchodilator FEV1. The study was terminated during Period 2; no data were collected for this endpoint at Week 104.

Reporting Groups

	Description
Navarixin 10 mg	Participants receive navarixin 10 mg, as one navarixin 10 mg capsule and two placebo capsules, administered orally QD for up to 2 years
Navarixin 30 mg	Participants receive navarixin 30 mg, as one navarixin 30 mg capsule and two placebo capsules, administered orally QD for up to 2 years
Navarixin 50 mg	Participants receive navarixin 50 mg, as two navarixin 10 mg capsules and one navarixin 30 mg capsule, administered orally QD for up to 2 years
Placebo	Participants receive placebo to navarixin, as three placebo capsules, administered orally QD for up to 2 years

Measured Values

	Navarixin 10 mg	Navarixin 30 mg	Navarixin 50 mg	Placebo
Number of Participants Analyzed [units: participants]	**124**	**104**	**103**	**126**
Change From Baseline in Pre-bronchodilator FEV1 [units: Liters] Least Squares Mean (Standard Error)				
Change at Week 26 (n=124, 104, 103 126)	**-0.035 (0.021)**	**-0.084 (0.022)**	**0.008 (0.022)**	**-0.054 (0.021)**
Change at Week 52 (n=65, 47, 43, 67)	**-0.049 (0.025)**	**-0.084 (0.028)**	**0.019 (0.029)**	**-0.073 (0.025)**
Change at Week 104 (n=0, 0, 0, 0)	**NA [1]**	**NA [1]**	**NA [1]**	**NA [1]**

[1] Study terminated; data not collected.

No statistical analysis provided for Change From Baseline in Pre-bronchodilator FEV1

11. Secondary: Change From Baseline in Forced Expiratory Flow During the Middle Half of the Forced Vital Capacity (FEF25%–75%) Test [Time Frame: Baseline and Week 26, Week 52, Week 104]

Measure Type	Secondary
Measure Title	Change From Baseline in Forced Expiratory Flow During the Middle Half of the Forced Vital Capacity (FEF25%–75%) Test
Measure Description	Mid-Breath Forced Expiratory Flow (FEF25%-75%), as measured in liters/minute by spirometry, is the rate at which participants breathe out air from 25 percent of their breath to 75 percent of their breath. FEF25%-75% was to be assessed at Baseline, Week 26, Week 52 and Week 104.
Time Frame	Baseline and Week 26, Week 52, Week 104
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The FAS population consisted of all participants who received at least one dose of study drug and had a Baseline and Week 26, Week 52 or Week 104 assessment for FEF25%-75%. The study was terminated during Period 2; no data were collected for this endpoint at Week 104.

Reporting Groups

	Description
Navarixin 10 mg	Participants receive navarixin 10 mg, as one navarixin 10 mg capsule and two placebo capsules, administered orally QD for up to 2 years
Navarixin 30 mg	Participants receive navarixin 30 mg, as one navarixin 30 mg capsule and two placebo capsules, administered orally QD for up to 2 years
Navarixin 50 mg	Participants receive navarixin 50 mg, as two navarixin 10 mg capsules and one navarixin 30 mg capsule, administered orally QD for up to 2 years
Placebo	Participants receive placebo to navarixin, as three placebo capsules, administered orally QD for up to 2 years

Measured Values

	Navarixin 10 mg	Navarixin 30 mg	Navarixin 50 mg	Placebo
Number of Participants Analyzed [units: participants]	**124**	**105**	**102**	**127**
Change From Baseline in Forced Expiratory Flow During the Middle Half of the Forced Vital Capacity (FEF25%–75%) Test [units: Liters/minute] Least Squares Mean (Standard Error)				
Change at Week 26 (n=124, 105, 102, 127)	**0.000 (0.016)**	**-0.053 (0.017)**	**0.028 (0.017)**	**-0.022 (0.016)**
Change at Week 52 (n=66, 47, 44, 65)	**-0.008 (0.020)**	**-0.055 (0.022)**	**0.031 (0.023)**	**-0.018 (0.020)**
Change at Week 104 (n=0, 0, 0, 0)	**NA [1]**	**NA [1]**	**NA [1]**	**NA [1]**

[1] Study terminated; data not collected.

No statistical analysis provided for Change From Baseline in Forced Expiratory Flow During the Middle Half of the Forced Vital Capacity (FEF25%–75%) Test

12. Secondary: Change From Baseline in Post-bronchodilator Forced Vital Capacity (FVC) [Time Frame: Baseline and Week 26, Week 52, Week 104]

Measure Type	Secondary
Measure Title	Change From Baseline in Post-bronchodilator Forced Vital Capacity (FVC)
Measure Description	FVC, as measured in liters by spirometry, is the amount of air forcibly exhaled from the lungs after taking the deepest breath possible. Post-bronchodilator FVC was to be assessed 30 minutes after bronchodilator administration (4 puffs of albuterol/salbutamol or equivalent separated by 30-second intervals) at Baseline, Week 26, Week 52 and Week 104.
Time Frame	Baseline and Week 26, Week 52, Week 104
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The FAS population consisted of all participants who received at least one dose of study drug and had a Baseline and Week 26, Week 52 or Week 104 assessment for post-bronchodilator FVC. The study was terminated during Period 2; no data were collected for this endpoint at Week 104.

Reporting Groups

	Description
Navarixin 10 mg	Participants receive navarixin 10 mg, as one navarixin 10 mg capsule and two placebo capsules, administered orally QD for up to 2 years
Navarixin 30 mg	Participants receive navarixin 30 mg, as one navarixin 30 mg capsule and two placebo capsules, administered orally QD for up to 2 years
Navarixin 50 mg	Participants receive navarixin 50 mg, as two navarixin 10 mg capsules and one navarixin 30 mg capsule, administered orally QD for up to 2 years
Placebo	Participants receive placebo to navarixin, as three placebo capsules, administered orally QD for up to 2 years

Measured Values

	Navarixin 10 mg	Navarixin 30 mg	Navarixin 50 mg	Placebo
Number of Participants Analyzed [units: participants]	**124**	**105**	**102**	**127**
Change From Baseline in Post-bronchodilator Forced Vital Capacity (FVC) [units: Liters] Least Squares Mean (Standard Error)				
Change at Week 26 (n=124, 105, 102, 127)	**-0.020 (0.040)**	**-0.089 (0.042)**	**-0.009 (0.043)**	**-0.086 (0.039)**
Change at Week 52 (n=66, 47, 44, 65)	**-0.106 (0.050)**	**-0.077 (0.057)**	**0.039 (0.059)**	**-0.057 (0.050)**
Change at Week 104 (n=0, 0, 0, 0)	**NA [1]**	**NA [1]**	**NA [1]**	**NA [1]**

[1] Study terminated; data not collected.

No statistical analysis provided for Change From Baseline in Post-bronchodilator Forced Vital Capacity (FVC)

13. Secondary: Change From Baseline in Functional Residual Capacity (FRC) [Time Frame: Baseline and Week 26, Week 52, Week 104]

Measure Type	Secondary
Measure Title	Change From Baseline in Functional Residual Capacity (FRC)
Measure Description	FRC, as measured in liters by body plethysmography, is the volume of air present in the lungs at the end of passive expiration. FRC was to be assessed after post-bronchodilator spirometry tests were performed at Baseline, Week 26, Week 52 and Week 104.
Time Frame	Baseline and Week 26, Week 52, Week 104
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The FAS population consisted of all participants who received at least one dose of study drug and had a Baseline and Week 26, Week 52 or Week 104 assessment for FRC. The study was terminated during Period 2; no data were collected for this endpoint at Week 104.

Reporting Groups

	Description
Navarixin 10 mg	Participants receive navarixin 10 mg, as one navarixin 10 mg capsule and two placebo capsules, administered orally QD for up to 2 years
Navarixin 30 mg	Participants receive navarixin 30 mg, as one navarixin 30 mg capsule and two placebo capsules, administered orally QD for up to 2 years
Navarixin 50 mg	Participants receive navarixin 50 mg, as two navarixin 10 mg capsules and one navarixin 30 mg capsule, administered orally QD for up to 2 years
Placebo	Participants receive placebo to navarixin, as three placebo capsules, administered orally QD for up to 2 years

Measured Values

	Navarixin 10 mg	Navarixin 30 mg	Navarixin 50 mg	Placebo
Number of Participants Analyzed [units: participants]	**65**	**55**	**50**	**59**
Change From Baseline in Functional Residual Capacity (FRC) [units: Liters] Least Squares Mean (Standard Error)				
Change at Week 26 (n=65, 55, 50, 59)	**0.15 (0.11)**	**-0.11 (0.12)**	**-0.07 (0.12)**	**0.07 (0.11)**
Change at Week 52 (n=24, 21, 18, 21)	**0.21 (0.13)**	**0.12 (0.14)**	**0.10 (0.15)**	**0.13 (0.14)**
Change at Week 104 (n=0, 0, 0, 0)	**NA [1]**	**NA [1]**	**NA [1]**	**NA [1]**

[1] Study terminated; data not collected.

No statistical analysis provided for Change From Baseline in Functional Residual Capacity (FRC)

14. Secondary: Change From Baseline in Total Lung Capacity (TLC) [Time Frame: Baseline and Week 26, Week 52, Week 104]

Measure Type	Secondary
Measure Title	Change From Baseline in Total Lung Capacity (TLC)
Measure Description	TLC, as measured in liters by body plethysmography, is the most amount of air lungs can hold at the top of breathing in. TLC was to be assessed after post-bronchodilator spirometry tests were performed at Baseline, Week 26, Week 52 and Week 104.
Time Frame	Baseline and Week 26, Week 52, Week 104
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The FAS population consisted of all participants who received at least one dose of study drug and had a Baseline and Week 26, Week 52 or Week 104 assessment for TLC. The study was terminated during Period 2; no data were collected for this endpoint at Week 104.

Reporting Groups

	Description
Navarixin 10 mg	Participants receive navarixin 10 mg, as one navarixin 10 mg capsule and two placebo capsules, administered orally QD for up to 2 years
Navarixin 30 mg	Participants receive navarixin 30 mg, as one navarixin 30 mg capsule and two placebo capsules, administered orally QD for up to 2 years
Navarixin 50 mg	Participants receive navarixin 50 mg, as two navarixin 10 mg capsules and one navarixin 30 mg capsule, administered orally QD for up to 2 years
Placebo	Participants receive placebo to navarixin, as three placebo capsules, administered orally QD for up to 2 years

Measured Values

	Navarixin 10 mg	Navarixin 30 mg	Navarixin 50 mg	Placebo

Number of Participants Analyzed [units: participants]	**65**	**55**	**50**	**59**
Change From Baseline in Total Lung Capacity (TLC) **[units: Liters]** **Least Squares Mean (Standard Error)**				
Change at Week 26 (n=65, 55, 50, 59)	**0.11 (0.11)**	**-0.14 (0.12)**	**-0.06 (0.12)**	**0.03 (0.11)**
Change at Week 52 (n=24, 21, 18, 21)	**0.15 (0.13)**	**0.01 (0.14)**	**0.13 (0.15)**	**0.11 (0.14)**
Change at Week 104 (n=0, 0, 0, 0)	**NA [1]**	**NA [1]**	**NA [1]**	**NA [1]**

[1] Study terminated; data not collected.

No statistical analysis provided for Change From Baseline in Total Lung Capacity (TLC)

15. Secondary: Change From Baseline in Inspiratory Capacity (IC) [Time Frame: Baseline and Week 26, Week 52, Week 104]

Measure Type	Secondary
Measure Title	Change From Baseline in Inspiratory Capacity (IC)
Measure Description	IC, as measured in liters by body plethysmography, is the maximum amount of air inspired when taking a slow, full inspiration with no hesitation from a position of passive end-tidal expiration (i.e. FRC) to a position of maximal inspiration. IC was to be assessed after post-bronchodilator spirometry tests were performed at Baseline, Week 26, Week 52 and Week 104.
Time Frame	Baseline and Week 26, Week 52, Week 104
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The FAS population consisted of all participants who received at least one dose of study drug and had a Baseline and Week 26, Week 52 or Week 104 assessment for IC. The study was terminated during Period 2; no data were collected for this endpoint at Week 104.

Reporting Groups

	Description
Navarixin 10 mg	Participants receive navarixin 10 mg, as one navarixin 10 mg capsule and two placebo capsules, administered orally QD for up to 2 years
Navarixin 30 mg	Participants receive navarixin 30 mg, as one navarixin 30 mg capsule and two placebo capsules, administered orally QD for up to 2 years
Navarixin 50 mg	Participants receive navarixin 50 mg, as two navarixin 10 mg capsules and one navarixin 30 mg capsule, administered orally QD for up to 2 years
Placebo	Participants receive placebo to navarixin, as three placebo capsules, administered orally QD for up to 2 years

Measured Values

	Navarixin 10 mg	**Navarixin 30 mg**	**Navarixin 50 mg**	**Placebo**
Number of Participants Analyzed	**66**	**55**	**50**	**60**

[units: participants]				
Change From Baseline in Inspiratory Capacity (IC) **[units: Liters]** **Least Squares Mean (Standard Error)**				
Change at Week 26 (n=66, 55, 50, 60)	**-0.04 (0.05)**	**-0.05 (0.06)**	**0.01 (0.06)**	**-0.05 (0.06)**
Change at Week 52 (n=24, 21, 18, 21)	**-0.02 (0.08)**	**-0.12 (0.09)**	**0.04 (0.09)**	**0.02 (0.09)**
Change at Week 104 (n=0, 0, 0, 0)	**NA [1]**	**NA [1]**	**NA [1]**	**NA [1]**

[1] Study terminated; data not collected.

No statistical analysis provided for Change From Baseline in Inspiratory Capacity (IC)

16. Secondary: Change From Baseline in Morning Peak Expiratory Flow (PEF) [Time Frame: Baseline and Week 26, Week 52, Week 104]

Measure Type	Secondary
Measure Title	Change From Baseline in Morning Peak Expiratory Flow (PEF)
Measure Description	PEF, as measured in liters/minute with a peak flow meter, is the maximum speed of expiration. Participants were to perform at least 3 and up to 5 PEF measurements in the morning before taking study drug. PEF was to be assessed at Baseline, Week 26, Week 52 and Week 104.
Time Frame	Baseline and Week 26, Week 52, Week 104
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The FAS population consisted of all participants who received at least one dose of study drug and had a Baseline and Week 26, Week 52 or Week 104 assessment for PEF. The study was terminated during Period 2; no data were collected for this endpoint at Week 104.

Reporting Groups

	Description
Navarixin 10 mg	Participants receive navarixin 10 mg, as one navarixin 10 mg capsule and two placebo capsules, administered orally QD for up to 2 years
Navarixin 30 mg	Participants receive navarixin 30 mg, as one navarixin 30 mg capsule and two placebo capsules, administered orally QD for up to 2 years
Navarixin 50 mg	Participants receive navarixin 50 mg, as two navarixin 10 mg capsules and one navarixin 30 mg capsule, administered orally QD for up to 2 years
Placebo	Participants receive placebo to navarixin, as three placebo capsules, administered orally QD for up to 2 years

Measured Values

	Navarixin 10 mg	**Navarixin 30 mg**	**Navarixin 50 mg**	**Placebo**
Number of Participants Analyzed **[units: participants]**	**119**	**97**	**95**	**122**
Change From Baseline in Morning Peak Expiratory Flow (PEF)				

[units: Liters/minute] Least Squares Mean (Standard Error)				
Change at Week 26 (n=119, 97, 95, 122)	-14.7 (4.28)	-20.5 (4.50)	-11.6 (4.61)	-21.8 (4.26)
Change at Week 52 (n=61, 48, 43, 63)	-23.7 (9.69)	-22.9 (10.88)	-0.48 (11.50)	-26.2 (9.54)
Change at Week 104 (n=0, 0, 0, 0)	NA [1]	NA [1]	NA [1]	NA [1]

[1] Study terminated; data not collected.

No statistical analysis provided for Change From Baseline in Morning Peak Expiratory Flow (PEF)

17. Secondary: Change From Baseline in Body-Mass Index, Airflow Obstruction, Dyspnea, and Exercise Capacity (BODE) Index Score [Time Frame: Baseline and Week 26, Week 52, Week 104]

Measure Type	Secondary
Measure Title	Change From Baseline in Body-Mass Index, Airflow Obstruction, Dyspnea, and Exercise Capacity (BODE) Index Score
Measure Description	The BODE index is a composite score assessing COPD prognosis that consists of 4 variables that are individually scored: FEV1 percent predicted, 6-Minute Walk Test, Modified Medical Research Council (MMRC) dyspnea scale and body mass index (BMI). The FEV1 percent predicted was scored from ≥65% (0 points, less airway obstruction) to ≤35% (3 points, greater airway obstruction). The 6-Minute Walk Distance was scored from: ≥350 meters (0 points, good exercise capacity) to ≤149 meters (3 points, poor exercise capacity). The MMRC Dyspnea Scale was scored from: MMRC 0: Dyspneic on strenuous exercise (0 points) to MMRC 4: Cannot leave house; breathless on dressing/undressing (3 points). BMI was scored as: >21 (0 points) and ≤21 (1 point). Variable scores were summed to produce a BODE index score. BODE index scores could range from 0 to 10, with a higher score correlating with an increased risk of COPD mortality. BODE index scores were to be assessed at Baseline, Week 26, Week 52 and Week 104.
Time Frame	Baseline and Week 26, Week 52, Week 104
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The FAS population consisted of all participants at selected sites who received at least one dose of study drug and had a Baseline and Week 26, Week 52 or Week 104 assessment for BODE index score. The study was terminated during Period 2; no data were collected for this endpoint at Week 104.

Reporting Groups

	Description
Navarixin 10 mg	Participants receive navarixin 10 mg, as one navarixin 10 mg capsule and two placebo capsules, administered orally QD for up to 2 years
Navarixin 30 mg	Participants receive navarixin 30 mg, as one navarixin 30 mg capsule and two placebo capsules, administered orally QD for up to 2 years
Navarixin 50 mg	Participants receive navarixin 50 mg, as two navarixin 10 mg capsules and one navarixin 30 mg capsule, administered orally QD for up to 2 years
Placebo	Participants receive placebo to navarixin, as three placebo capsules, administered orally QD for up to 2 years

Measured Values

	Navarixin 10 mg	Navarixin 30 mg	Navarixin 50 mg	Placebo
Number of Participants Analyzed [units: participants]	**83**	**72**	**67**	**84**
Change From Baseline in Body-Mass Index, Airflow Obstruction, Dyspnea, and Exercise Capacity (BODE) Index Score [units: Score on a Scale] Least Squares Mean (Standard Error)				
Change at Week 26 (n=83, 72, 67, 84)	**-0.35 (0.12)**	**0.13 (0.13)**	**-0.21 (0.13)**	**0.07 (0.12)**
Change at Week 52 (n=31, 21, 23, 27)	**-0.10 (0.21)**	**-0.02 (0.25)**	**0.09 (0.24)**	**0.12 (0.22)**
Change at Week 104 (n=0, 0, 0, 0)	**NA [1]**	**NA [1]**	**NA [1]**	**NA [1]**

[1] Study terminated; data not collected.

No statistical analysis provided for Change From Baseline in Body-Mass Index, Airflow Obstruction, Dyspnea, and Exercise Capacity (BODE) Index Score

18. Secondary: Change From Baseline in Modified Medical Research Council (MMRC) Dyspnea Score [Time Frame: Baseline and Week 26, Week 52, Week 104]

Measure Type	Secondary
Measure Title	Change From Baseline in Modified Medical Research Council (MMRC) Dyspnea Score
Measure Description	The MMRC dyspnea scale is used to assess participant breathlessness. The MMRC dyspnea scale consists of five grades that describe almost the entire range of respiratory disability from none (Grade 0=Not troubled with breathlessness except with strenuous exercise) to almost complete incapacity (Grade 4=Too breathless to leave the house or breathless when dressing or undressing). MMRC dyspnea scores were to be assessed at Baseline, Week 26, Week 52 and Week 104.
Time Frame	Baseline and Week 26, Week 52, Week 104
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The FAS population consisted of all participants who received at least one dose of study drug and had a Baseline and Week 26, Week 52 or Week 104 assessment for MMRC dyspnea score. The study was terminated during Period 2; no data were collected for this endpoint at Week 104.

Reporting Groups

	Description
Navarixin 10 mg	Participants receive navarixin 10 mg, as one navarixin 10 mg capsule and two placebo capsules, administered orally QD for up to 2 years
Navarixin 30 mg	Participants receive navarixin 30 mg, as one navarixin 30 mg capsule and two placebo capsules, administered orally QD for up to 2 years
Navarixin 50 mg	Participants receive navarixin 50 mg, as two navarixin 10 mg capsules and one navarixin 30 mg capsule, administered orally QD for up to 2 years

Placebo	Participants receive placebo to navarixin, as three placebo capsules, administered orally QD for up to 2 years

Measured Values

	Navarixin 10 mg	Navarixin 30 mg	Navarixin 50 mg	Placebo
Number of Participants Analyzed [units: participants]	**83**	**75**	**68**	**86**
Change From Baseline in Modified Medical Research Council (MMRC) Dyspnea Score [units: Score on a Scale] Least Squares Mean (Standard Error)				
Change at Week 26 (n=83, 75, 68, 86)	**-0.34 (0.08)**	**-0.02 (0.09)**	**-0.24 (0.09)**	**-0.07 (0.08)**
Change at Week 52 (n=33, 28, 25, 31)	**-0.25 (0.15)**	**0.05 (0.16)**	**-0.09 (0.17)**	**-0.07 (0.15)**
Change at Week 104 (n=0, 0, 0, 0)	**NA [1]**	**NA [1]**	**NA [1]**	**NA [1]**

[1] Study terminated; data not collected.

No statistical analysis provided for Change From Baseline in Modified Medical Research Council (MMRC) Dyspnea Score

19. Secondary: Sputum Inflammatory Marker Levels: Interleukin 8 (IL-8) [Time Frame: Baseline, Week 26, Week 52, Week 104]

Measure Type	Secondary
Measure Title	Sputum Inflammatory Marker Levels: Interleukin 8 (IL-8)
Measure Description	Induced sputum samples were to be collected from participants via the nebulized method prior to study drug administration at Week 26, Week 52 and Week 104. IL-8 levels were measured by enzyme-linked immunosorbent assay (ELISA) in the sputum supernatant. The reported Baseline LS means and SDs are pooled across all treatment groups. The rationale for the use of pooled Baseline LS mean and SD values is the assumption that the Baseline LS mean and SD values are similar across treatment groups. The reported post-Baseline SDs are pooled across all treatment groups. The rationale for the use of an ANOVA method using pooled SD values is the assumption that the SDs are similar across treatment groups.
Time Frame	Baseline, Week 26, Week 52, Week 104
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The FAS population consisted of all participants at selected sites who received at least one dose of study drug and had a Week 26, Week 52 or Week 104 assessment for sputum IL-8 level. The study was terminated during Period 2; no data were collected for this endpoint at Weeks 52 or 104.

Reporting Groups

	Description
Navarixin 10 mg	Participants receive navarixin 10 mg, as one navarixin 10 mg capsule and two placebo capsules, administered orally QD for up to 2 years
Navarixin 30 mg	Participants receive navarixin 30 mg, as one navarixin 30 mg capsule and two placebo capsules, administered orally QD for up to 2 years

Navarixin 50 mg	Participants receive navarixin 50 mg, as two navarixin 10 mg capsules and one navarixin 30 mg capsule, administered orally QD for up to 2 years
Placebo	Participants receive placebo to navarixin, as three placebo capsules, administered orally QD for up to 2 years

Measured Values

	Navarixin 10 mg	Navarixin 30 mg	Navarixin 50 mg	Placebo
Number of Participants Analyzed [units: participants]	**38**	**36**	**48**	**42**
Sputum Inflammatory Marker Levels: Interleukin 8 (IL-8) [units: pg/mL] Least Squares Mean (Standard Deviation)				
Baseline (n=38, 36, 48, 42)	**29.736 (0.552)**	**29.736 (0.552)**	**29.736 (0.552)**	**29.736 (0.552)**
Week 26 (n=24, 22, 19, 21)	**35.392 (0.410)**	**38.471 (0.410)**	**31.693 (0.410)**	**30.421 (0.410)**
Week 52 (n=0, 0, 0, 0)	**NA [1]**	**NA [1]**	**NA [1]**	**NA [1]**
Week 104 (n=0, 0, 0, 0)	**NA [1]**	**NA [1]**	**NA [1]**	**NA [1]**

[1] Study terminated; data not collected.

No statistical analysis provided for Sputum Inflammatory Marker Levels: Interleukin 8 (IL-8)

20. Secondary: Sputum Inflammatory Marker Levels: Myeloperoxidase (MPO) [Time Frame: Baseline, Week 26, Week 52, Week 104]

Measure Type	Secondary
Measure Title	Sputum Inflammatory Marker Levels: Myeloperoxidase (MPO)
Measure Description	Induced sputum samples were to be collected from participants via the nebulized method prior to study drug administration at Week 26, Week 52 and Week 104. MPO levels were measured by ELISA in the sputum supernatant. The reported Baseline LS means and SDs are pooled across all treatment groups. The rationale for the use of pooled Baseline LS mean and SD values is the assumption that the Baseline LS mean and SD values are similar across treatment groups. The reported post-Baseline SDs are pooled across all treatment groups. The rationale for the use of an ANOVA method using pooled SD values is the assumption that the SDs are similar across treatment groups.
Time Frame	Baseline, Week 26, Week 52, Week 104
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The FAS population consisted of all participants at selected sites who received at least one dose of study drug and had a Week 26, Week 52 or Week 104 assessment for sputum MPO level. The study was terminated during Period 2; no data were collected for this endpoint at Weeks 52 or 104.

Reporting Groups

	Description
Navarixin 10 mg	Participants receive navarixin 10 mg, as one navarixin 10 mg capsule and two placebo capsules, administered orally QD for up to 2 years

Navarixin 30 mg	Participants receive navarixin 30 mg, as one navarixin 30 mg capsule and two placebo capsules, administered orally QD for up to 2 years
Navarixin 50 mg	Participants receive navarixin 50 mg, as two navarixin 10 mg capsules and one navarixin 30 mg capsule, administered orally QD for up to 2 years
Placebo	Participants receive placebo to navarixin, as three placebo capsules, administered orally QD for up to 2 years

Measured Values

	Navarixin 10 mg	Navarixin 30 mg	Navarixin 50 mg	Placebo
Number of Participants Analyzed [units: participants]	**37**	**36**	**45**	**41**
Sputum Inflammatory Marker Levels: Myeloperoxidase (MPO) [units: ng/mL] Least Squares Mean (Standard Deviation)				
Baseline (n=37, 36, 45, 41)	**1.840 (1.120)**	**1.840 (1.120)**	**1.840 (1.120)**	**1.840 (1.120)**
Week 26 (n=24, 22, 19, 20)	**3.243 (1.488)**	**1.747 (1.488)**	**0.932 (1.488)**	**3.656 (1.488)**
Week 52 (n=0, 0, 0, 0)	**NA** [1]	**NA** [1]	**NA** [1]	**NA** [1]
Week 104 (n=0, 0, 0, 0)	**NA** [1]	**NA** [1]	**NA** [1]	**NA** [1]

[1] Study terminated; data not collected.

No statistical analysis provided for Sputum Inflammatory Marker Levels: Myeloperoxidase (MPO)

21. Secondary: Sputum Inflammatory Marker Levels: Sputum Neutrophil Elastase [Time Frame: Baseline, Week 26, Week 52, Week 104]

Measure Type	Secondary
Measure Title	Sputum Inflammatory Marker Levels: Sputum Neutrophil Elastase
Measure Description	Induced sputum samples were to be collected from participants via the nebulized method prior to study drug administration at Week 26, Week 52 and Week 104. Neutrophil elastase levels were measured in the sputum supernatant. The reported Baseline LS means and SDs are pooled across all treatment groups. The rationale for the use of pooled Baseline LS mean and SD values is the assumption that the Baseline LS mean and SD values are similar across treatment groups. The reported post-Baseline SDs are pooled across all treatment groups. The rationale for the use of an ANOVA method using pooled SD values is the assumption that the SDs are similar across treatment groups.
Time Frame	Baseline, Week 26, Week 52, Week 104
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The FAS population consisted of all participants at selected sites who received at least one dose of study drug and had a Week 26, Week 52 or Week 104 assessment for sputum neutrophil elastase level. The study was terminated during Period 2; no data were collected for this endpoint at Weeks 52 or 104.

Reporting Groups

	Description
Navarixin 10 mg	Participants receive navarixin 10 mg, as one navarixin 10 mg capsule and two placebo capsules, administered orally QD for up to 2 years
Navarixin 30 mg	Participants receive navarixin 30 mg, as one navarixin 30 mg capsule and two placebo capsules, administered orally QD for up to 2 years
Navarixin 50 mg	Participants receive navarixin 50 mg, as two navarixin 10 mg capsules and one navarixin 30 mg capsule, administered orally QD for up to 2 years
Placebo	Participants receive placebo to navarixin, as three placebo capsules, administered orally QD for up to 2 years

Measured Values

	Navarixin 10 mg	Navarixin 30 mg	Navarixin 50 mg	Placebo
Number of Participants Analyzed [units: participants]	**36**	**34**	**43**	**37**
Sputum Inflammatory Marker Levels: Sputum Neutrophil Elastase [units: ng/mL] Least Squares Mean (Standard Deviation)				
Baseline (n=36, 34, 43, 37)	**16.948 (0.700)**	**16.948 (0.700)**	**16.948 (0.700)**	**16.948 (0.700)**
Week 26 (n=23, 17, 19, 19)	**16.785 (0.773)**	**11.365 (0.773)**	**19.106 (0.773)**	**27.973 (0.773)**
Week 52 (n=0, 0, 0, 0)	**NA** [1]	**NA** [1]	**NA** [1]	**NA** [1]
Week 104 (n=0, 0, 0, 0)	**NA** [1]	**NA** [1]	**NA** [1]	**NA** [1]

[1] Study terminated; data not collected.

No statistical analysis provided for Sputum Inflammatory Marker Levels: Sputum Neutrophil Elastase

22. Secondary: Sputum Inflammatory Marker Levels: Matrix Metallopeptidase-9 (MMP-9) [Time Frame: Baseline, Week 26, Week 52, Week 104]

Measure Type	Secondary
Measure Title	Sputum Inflammatory Marker Levels: Matrix Metallopeptidase-9 (MMP-9)
Measure Description	Induced sputum samples were to be collected from participants via the nebulized method prior to study drug administration at Week 26, Week 52 and Week 104. MMP-9 levels were measured by ELISA in the sputum supernatant. The reported Baseline LS means and SDs are pooled across all treatment groups. The rationale for the use of pooled Baseline LS mean and SD values is the assumption that the Baseline LS mean and SD values are similar across treatment groups. The reported post-Baseline SDs are pooled across all treatment groups. The rationale for the use of an ANOVA method using pooled SD values is the assumption that the SDs are similar across treatment groups.
Time Frame	Baseline, Week 26, Week 52, Week 104
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The FAS population consisted of all participants at selected sites who received at least one dose of study drug and had a Week 26, Week 52 or

Week 104 assessment for induced sputum MMP-9 level. The study was terminated during Period 2; no data were collected for this endpoint at Weeks 52 or 104.

Reporting Groups

	Description
Navarixin 10 mg	Participants receive navarixin 10 mg, as one navarixin 10 mg capsule and two placebo capsules, administered orally QD for up to 2 years
Navarixin 30 mg	Participants receive navarixin 30 mg, as one navarixin 30 mg capsule and two placebo capsules, administered orally QD for up to 2 years
Navarixin 50 mg	Participants receive navarixin 50 mg, as two navarixin 10 mg capsules and one navarixin 30 mg capsule, administered orally QD for up to 2 years
Placebo	Participants receive placebo to navarixin, as three placebo capsules, administered orally QD for up to 2 years

Measured Values

	Navarixin 10 mg	Navarixin 30 mg	Navarixin 50 mg	Placebo
Number of Participants Analyzed [units: participants]	**39**	**35**	**46**	**41**
Sputum Inflammatory Marker Levels: Matrix Metallopeptidase-9 (MMP-9) [units: ng/mL] Least Squares Mean (Standard Deviation)				
Baseline (n=39, 35, 46, 41)	**720.45 (0.773)**	**720.45 (0.773)**	**720.45 (0.773)**	**720.45 (0.773)**
Week 26 (n=24, 22, 19, 21)	**878.02 (0.709)**	**711.90 (0.709)**	**392.81 (0.709)**	**1480.1 (0.709)**
Week 52 (n=0, 0, 0, 0)	**NA** [1]	**NA** [1]	**NA** [1]	**NA** [1]
Week 104 (n=0, 0, 0, 0)	**NA** [1]	**NA** [1]	**NA** [1]	**NA** [1]

[1] Study terminated; data not collected.

No statistical analysis provided for Sputum Inflammatory Marker Levels: Matrix Metallopeptidase-9 (MMP-9)

23. Secondary: Plasma Inflammatory Biomarker Levels: High-sensitivity C-reactive Protein (Hs-CRP) [Time Frame: Baseline, Week 26, Week 52, Week 104]

Measure Type	Secondary
Measure Title	Plasma Inflammatory Biomarker Levels: High-sensitivity C-reactive Protein (Hs-CRP)
Measure Description	Blood samples were to be collected prior to study drug administration to determine participant plasma hs-CRP levels at Week 26, Week 52 and Week 104. The reported Baseline LS means and SDs are pooled across all treatment groups. The rationale for the use of pooled Baseline LS mean and SD values is the assumption that the Baseline LS mean and SD values are similar across treatment groups. The reported post-Baseline SDs are pooled across all treatment groups. The rationale for the use of an ANOVA method using pooled SD values is the assumption that the SDs are similar across treatment groups.
Time Frame	Baseline, Week 26, Week 52, Week 104
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The FAS population consisted of all participants who received at least one dose of study drug and had a Week 26, Week 52 or Week 104 assessment for plasma hs-CRP level. The study was terminated during Period 2; no data were collected for this endpoint at Week 104.

Reporting Groups

	Description
Navarixin 10 mg	Participants receive navarixin 10 mg, as one navarixin 10 mg capsule and two placebo capsules, administered orally QD for up to 2 years
Navarixin 30 mg	Participants receive navarixin 30 mg, as one navarixin 30 mg capsule and two placebo capsules, administered orally QD for up to 2 years
Navarixin 50 mg	Participants receive navarixin 50 mg, as two navarixin 10 mg capsules and one navarixin 30 mg capsule, administered orally QD for up to 2 years
Placebo	Participants receive placebo to navarixin, as three placebo capsules, administered orally QD for up to 2 years

Measured Values

	Navarixin 10 mg	**Navarixin 30 mg**	**Navarixin 50 mg**	**Placebo**
Number of Participants Analyzed [units: participants]	**148**	**152**	**149**	**150**
Plasma Inflammatory Biomarker Levels: High-sensitivity C-reactive Protein (Hs-CRP) [units: mg/dL] Least Squares Mean (Standard Deviation)				
Baseline (n=148, 152, 149, 150)	**2.766 (0.498)**	**2.766 (0.498)**	**2.766 (0.498)**	**2.766 (0.498)**
Week 26 (n=121, 104, 100, 126)	**2.832 (0.443)**	**3.728 (0.443)**	**4.410 (0.443)**	**2.889 (0.443)**
Week 52 (n=67, 49, 43, 68)	**3.360 (0.432)**	**3.871 (0.432)**	**4.566 (0.432)**	**2.657 (0.432)**
Week 104 (n=0, 0, 0, 0)	**NA** [1]	**NA** [1]	**NA** [1]	**NA** [1]

[1] Study terminated; data not collected.

No statistical analysis provided for Plasma Inflammatory Biomarker Levels: High-sensitivity C-reactive Protein (Hs-CRP)

24. Secondary: Plasma Inflammatory Biomarker Levels: Fibrinogen [Time Frame: Baseline, Week 26, Week 52, Week 104]

Measure Type	Secondary
Measure Title	Plasma Inflammatory Biomarker Levels: Fibrinogen
Measure Description	Blood samples were to be collected prior to study drug administration to determine participant plasma fibrinogen levels at Week 26, Week 52 and Week 104. The reported Baseline LS means and SDs are pooled across all treatment groups. The rationale for the use of pooled Baseline LS mean and SD values is the assumption that the Baseline LS mean and SD values are similar across treatment groups. The reported post-Baseline SDs are pooled across all treatment groups. The rationale for the use of an ANOVA method using pooled SD values is the assumption that the SDs are similar across treatment groups.
Time Frame	Baseline, Week 26, Week 52, Week 104

Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The FAS population consisted of all participants who received at least one dose of study drug and had a Week 26, Week 52 or Week 104 assessment for plasma fibrinogen level. The study was terminated during Period 2; no data were collected for this endpoint at Week 104.

Reporting Groups

	Description
Navarixin 10 mg	Participants receive navarixin 10 mg, as one navarixin 10 mg capsule and two placebo capsules, administered orally QD for up to 2 years
Navarixin 30 mg	Participants receive navarixin 30 mg, as one navarixin 30 mg capsule and two placebo capsules, administered orally QD for up to 2 years
Navarixin 50 mg	Participants receive navarixin 50 mg, as two navarixin 10 mg capsules and one navarixin 30 mg capsule, administered orally QD for up to 2 years
Placebo	Participants receive placebo to navarixin, as three placebo capsules, administered orally QD for up to 2 years

Measured Values

	Navarixin 10 mg	**Navarixin 30 mg**	**Navarixin 50 mg**	**Placebo**
Number of Participants Analyzed [units: participants]	**140**	**138**	**138**	**143**
Plasma Inflammatory Biomarker Levels: Fibrinogen [units: mg/dL] Least Squares Mean (Standard Deviation)				
Baseline (n=140, 138, 138, 143)	**3.731 (0.108)**	**3.731 (0.108)**	**3.731 (0.108)**	**3.731 (0.108)**
Week 26 (n=111, 104, 91, 121)	**3.835 (0.119)**	**4.027 (0.119)**	**4.068 (0.119)**	**3.788 (0.119)**
Week 52 (n=52, 40, 38, 58)	**4.163 (0.108)**	**4.031 (0.108)**	**4.308 (0.108)**	**3.788 (0.108)**
Week 104 (n=0, 0, 0, 0)	**NA [1]**	**NA [1]**	**NA [1]**	**NA [1]**

[1] Study terminated; data not collected.

No statistical analysis provided for Plasma Inflammatory Biomarker Levels: Fibrinogen

25. Secondary: Plasma Inflammatory Biomarker Levels: Myeloperoxidase (MPO) [Time Frame: Baseline, Week 26, Week 52, Week 104]

Measure Type	Secondary
Measure Title	Plasma Inflammatory Biomarker Levels: Myeloperoxidase (MPO)
Measure Description	Blood samples were to be collected prior to study drug administration to determine participant plasma MPO levels at Week 26, Week 52 and Week 104. The reported Baseline LS means and SDs are pooled across all treatment groups. The rationale for the use of pooled Baseline LS mean and SD values is the assumption that the Baseline LS mean and SD values are similar across treatment groups. The reported post-Baseline SDs are pooled across all treatment groups. The rationale for the use of an ANOVA method using pooled SD values is the assumption that the SDs are similar

	across treatment groups.
Time Frame	Baseline, Week 26, Week 52, Week 104
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The FAS population consisted of all participants who received at least one dose of study drug and had a Week 26, Week 52 or Week 104 assessment for MPO level. The study was terminated during Period 2; no data were collected for this endpoint at Week 104.

Reporting Groups

	Description
Navarixin 10 mg	Participants receive navarixin 10 mg, as one navarixin 10 mg capsule and two placebo capsules, administered orally QD for up to 2 years
Navarixin 30 mg	Participants receive navarixin 30 mg, as one navarixin 30 mg capsule and two placebo capsules, administered orally QD for up to 2 years
Navarixin 50 mg	Participants receive navarixin 50 mg, as two navarixin 10 mg capsules and one navarixin 30 mg capsule, administered orally QD for up to 2 years
Placebo	Participants receive placebo to navarixin, as three placebo capsules, administered orally QD for up to 2 years

Measured Values

	Navarixin 10 mg	**Navarixin 30 mg**	**Navarixin 50 mg**	**Placebo**
Number of Participants Analyzed [units: participants]	**146**	**145**	**147**	**148**
Plasma Inflammatory Biomarker Levels: Myeloperoxidase (MPO) [units: ng/mL] Least Squares Mean (Standard Deviation)				
Baseline (n=146, 145, 147, 148)	**169.15 (0.386)**	**169.15 (0.386)**	**169.15 (0.386)**	**169.15 (0.386)**
Week 26 (n=119, 104, 97, 124)	**188.70 (0.439)**	**175.80 (0.439)**	**173.16 (0.439)**	**227.72 (0.439)**
Week 52 (n=47, 36, 35, 46)	**234.42 (0.451)**	**196.67 (0.451)**	**246.04 (0.451)**	**254.20 (0.451)**
Week 104 (n=0, 0, 0, 0)	**NA [1]**	**NA [1]**	**NA [1]**	**NA [1]**

[1] Study terminated; data not collected.

No statistical analysis provided for Plasma Inflammatory Biomarker Levels: Myeloperoxidase (MPO)

26. Secondary: Plasma Inflammatory Biomarker Levels: Matrix Metallopeptidase-9 (MMP-9) [Time Frame: Baseline, Week 26, Week 52, Week 104]

Measure Type	Secondary
Measure Title	Plasma Inflammatory Biomarker Levels: Matrix Metallopeptidase-9 (MMP-9)
Measure Description	Blood samples were to be collected prior to study drug administration to determine participant plasma MMP-9 levels at

	Week 26, Week 52 and Week 104. The reported Baseline LS means and SDs are pooled across all treatment groups. The rationale for the use of pooled Baseline LS mean and SD values is the assumption that the Baseline LS mean and SD values are similar across treatment groups. The reported post-Baseline SDs are pooled across all treatment groups. The rationale for the use of an ANOVA method using pooled SD values is the assumption that the SDs are similar across treatment groups.
Time Frame	Baseline, Week 26, Week 52, Week 104
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The FAS population consisted of all participants who received at least one dose of study drug and had a Week 26, Week 52 or Week 104 assessment for MMP-9 level. The study was terminated during Period 2; no data were collected for this endpoint at Week 104.

Reporting Groups

	Description
Navarixin 10 mg	Participants receive navarixin 10 mg, as one navarixin 10 mg capsule and two placebo capsules, administered orally QD for up to 2 years
Navarixin 30 mg	Participants receive navarixin 30 mg, as one navarixin 30 mg capsule and two placebo capsules, administered orally QD for up to 2 years
Navarixin 50 mg	Participants receive navarixin 50 mg, as two navarixin 10 mg capsules and one navarixin 30 mg capsule, administered orally QD for up to 2 years
Placebo	Participants receive placebo to navarixin, as three placebo capsules, administered orally QD for up to 2 years

Measured Values

	Navarixin 10 mg	**Navarixin 30 mg**	**Navarixin 50 mg**	**Placebo**
Number of Participants Analyzed [units: participants]	**146**	**145**	**147**	**148**
Plasma Inflammatory Biomarker Levels: Matrix Metallopeptidase-9 (MMP-9) [units: ng/mL] Least Squares Mean (Standard Deviation)				
Baseline (n=146, 145, 147, 148)	**294.80 (0.254)**	**294.80 (0.254)**	**294.80 (0.254)**	**294.80 (0.254)**
Week 26 (n=119, 104, 97, 124)	**247.63 (0.272)**	**216.40 (0.272)**	**217.79 (0.272)**	**319.80 (0.272)**
Week 52 (n=48, 36, 35, 47)	**258.82 (0.272)**	**220.90 (0.272)**	**244.67 (0.272)**	**342.46 (0.272)**
Week 104 (n=0, 0, 0, 0)	**NA** [1]	**NA** [1]	**NA** [1]	**NA** [1]

[1] Study terminated; data not collected.

No statistical analysis provided for Plasma Inflammatory Biomarker Levels: Matrix Metallopeptidase-9 (MMP-9)

27. Secondary: Plasma Inflammatory Biomarker Levels: Plasma Neutrophil Elastase [Time Frame: Baseline, Week 26, Week 52, Week 104]

Measure Type	Secondary

Measure Title	Plasma Inflammatory Biomarker Levels: Plasma Neutrophil Elastase
Measure Description	Blood samples were to be collected prior to study drug administration to determine participant plasma neutrophil elastase levels at Week 26, Week 52 and Week 104. The reported Baseline LS means and SDs are pooled across all treatment groups. The rationale for the use of pooled Baseline LS mean and SD values is the assumption that the Baseline LS mean and SD values are similar across treatment groups. The reported post-Baseline SDs are pooled across all treatment groups. The rationale for the use of an ANOVA method using pooled SD values is the assumption that the SDs are similar across treatment groups.
Time Frame	Baseline, Week 26, Week 52, Week 104
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The FAS population consisted of all participants who received at least one dose of study drug and had a Week 26, Week 52 or Week 104 assessment for plasma neutrophil elastase level. The study was terminated during Period 2; no data were collected for the endpoint at Week 104.

Reporting Groups

	Description
Navarixin 10 mg	Participants receive navarixin 10 mg, as one navarixin 10 mg capsule and two placebo capsules, administered orally QD for up to 2 years
Navarixin 30 mg	Participants receive navarixin 30 mg, as one navarixin 30 mg capsule and two placebo capsules, administered orally QD for up to 2 years
Navarixin 50 mg	Participants receive navarixin 50 mg, as two navarixin 10 mg capsules and one navarixin 30 mg capsule, administered orally QD for up to 2 years
Placebo	Participants receive placebo to navarixin, as three placebo capsules, administered orally QD for up to 2 years

Measured Values

	Navarixin 10 mg	**Navarixin 30 mg**	**Navarixin 50 mg**	**Placebo**
Number of Participants Analyzed [units: participants]	**123**	**117**	**122**	**121**
Plasma Inflammatory Biomarker Levels: Plasma Neutrophil Elastase [units: ng/mL] Least Squares Mean (Standard Deviation)				
Baseline (n=123, 117, 122, 121)	**67.969 (0.323)**	**67.969 (0.323)**	**67.969 (0.323)**	**67.969 (0.323)**
Week 26 (n=118, 104, 93, 121)	**63.592 (0.341)**	**63.680 (0.341)**	**65.413 (0.341)**	**67.697 (0.341)**
Week 52 (n=51, 41, 33, 52)	**60.965 (0.280)**	**54.267 (0.280)**	**64.296 (0.280)**	**57.804 (0.280)**
Week 104 (n=0, 0, 0, 0)	**NA [1]**	**NA [1]**	**NA [1]**	**NA [1]**

[1] Study terminated; data not collected.

No statistical analysis provided for Plasma Inflammatory Biomarker Levels: Plasma Neutrophil Elastase

28. Secondary: Plasma Inflammatory Biomarker Levels: Epithelial Cell-Derived Neutrophil Activating Peptide 78 (ENA-78) [Time Frame: Baseline, Week 26, Week 52, Week 104]

Measure Type	Secondary
Measure Title	Plasma Inflammatory Biomarker Levels: Epithelial Cell-Derived Neutrophil Activating Peptide 78 (ENA-78)
Measure Description	Blood samples were to be collected prior to study drug administration to determine participant plasma ENA-78 levels at Week 26, Week 52 and Week 104. The reported Baseline LS means and SDs are pooled across all treatment groups. The rationale for the use of pooled Baseline LS mean and SD values is the assumption that the Baseline LS mean and SD values are similar across treatment groups. The reported post-Baseline SDs are pooled across all treatment groups. The rationale for the use of an ANOVA method using pooled SD values is the assumption that the SDs are similar across treatment groups.
Time Frame	Baseline, Week 26, Week 52, Week 104
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The FAS population consisted of all participants who received at least one dose of study drug and had a Week 26, Week 52 or Week 104 assessment for ENA-78 level. The study was terminated during Period 2; no data were collected for this endpoint at Week 104.

Reporting Groups

	Description
Navarixin 10 mg	Participants receive navarixin 10 mg, as one navarixin 10 mg capsule and two placebo capsules, administered orally QD for up to 2 years
Navarixin 30 mg	Participants receive navarixin 30 mg, as one navarixin 30 mg capsule and two placebo capsules, administered orally QD for up to 2 years
Navarixin 50 mg	Participants receive navarixin 50 mg, as two navarixin 10 mg capsules and one navarixin 30 mg capsule, administered orally QD for up to 2 years
Placebo	Participants receive placebo to navarixin, as three placebo capsules, administered orally QD for up to 2 years

Measured Values

	Navarixin 10 mg	**Navarixin 30 mg**	**Navarixin 50 mg**	**Placebo**
Number of Participants Analyzed [units: participants]	**125**	**118**	**122**	**126**
Plasma Inflammatory Biomarker Levels: Epithelial Cell-Derived Neutrophil Activating Peptide 78 (ENA-78) [units: pg/mL] Least Squares Mean (Standard Deviation)				
Baseline (n=125, 118, 122, 126)	**436.31 (0.430)**	**436.31 (0.430)**	**436.31 (0.430)**	**436.31 (0.430)**
Week 26 (n=119, 105, 92, 121)	**508.31 (0.451)**	**543.60 (0.451)**	**607.37 (0.451)**	**473.10 (0.451)**
Week 52 (n=42, 32, 33, 42)	**509.93 (0.409)**	**603.44 (0.409)**	**698.93 (0.409)**	**417.90 (0.409)**
Week 104 (n=0, 0, 0, 0)	**NA [1]**	**NA [1]**	**NA [1]**	**NA [1]**

[1] Study terminated; data not collected.

No statistical analysis provided for Plasma Inflammatory Biomarker Levels: Epithelial Cell-Derived Neutrophil Activating Peptide 78 (ENA-78)

29. Secondary: Change From Baseline in Pre- and Post-6-Minute-Walk-Test Borg Scale Score [Time Frame: Baseline and Week 26, Week 52, Week 104]

Measure Type	Secondary
Measure Title	Change From Baseline in Pre- and Post-6-Minute-Walk-Test Borg Scale Score
Measure Description	The 6-minute walk test measured the distance participants could walk quickly on a flat, hard surface in 6 minutes. The Borg scale is a method use to rate perceived exertion (0=Nothing at all [no exertion] to 10=Maximal [exertion]). Borg scale scores were to be assessed pre- and post-walk-test at Baseline, Week 26, Week 52 and Week 104. A higher score indicates greater perceived exertion.
Time Frame	Baseline and Week 26, Week 52, Week 104
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The FAS population consisted of all participants at selected sites who received at least one dose of study drug and had a Baseline and Week 26, Week 52 or Week 104 assessment for pre- and post-6-minute-walk-test Borg scale score. The study was terminated during Period 2; no data were collected for this endpoint at Week 104.

Reporting Groups

	Description
Navarixin 10 mg	Participants receive navarixin 10 mg, as one navarixin 10 mg capsule and two placebo capsules, administered orally QD for up to 2 years
Navarixin 30 mg	Participants receive navarixin 30 mg, as one navarixin 30 mg capsule and two placebo capsules, administered orally QD for up to 2 years
Navarixin 50 mg	Participants receive navarixin 50 mg, as two navarixin 10 mg capsules and one navarixin 30 mg capsule, administered orally QD for up to 2 years
Placebo	Participants receive placebo to navarixin, as three placebo capsules, administered orally QD for up to 2 years

Measured Values

	Navarixin 10 mg	**Navarixin 30 mg**	**Navarixin 50 mg**	**Placebo**
Number of Participants Analyzed [units: participants]	**84**	**77**	**68**	**87**
Change From Baseline in Pre- and Post-6-Minute-Walk-Test Borg Scale Score [units: Score on a Scale] Least Squares Mean (Standard Error)				
Pre-walk Change at Week 26 (n=84, 77, 68, 87)	**-0.27 (0.12)**	**0.07 (0.12)**	**-0.13 (0.13)**	**0.17 (0.12)**
Pre-walk Change at Week 52 (n=32, 25, 25, 30)	**-0.18 (0.19)**	**0.22 (0.21)**	**0.08 (0.21)**	**0.21 (0.20)**
Post-walk Change at Week 26 (n=84, 77, 68, 87)	**-0.52 (0.14)**	**-0.03 (0.15)**	**0.10 (0.16)**	**0.11 (0.14)**

Post-walk Change at Week 52 (n=32, 25, 25, 30)	**-0.26 (0.26)**	**0.52 (0.29)**	**-0.16 (0.30)**	**0.26 (0.27)**
Pre-walk Change at Week 104 (n=0, 0, 0, 0)	**NA [1]**	**NA [1]**	**NA [1]**	**NA [1]**
Post-walk Change at Week 104 (n=0, 0, 0, 0)	**NA [1]**	**NA [1]**	**NA [1]**	**NA [1]**

[1] Study terminated; data not collected.

No statistical analysis provided for Change From Baseline in Pre- and Post-6-Minute-Walk-Test Borg Scale Score

30. Secondary: Change From Baseline in Percent of Arterial Oxygen Saturation Measured by Pulse Oximetry Before and After the 6-Minute Walk Test [Time Frame: Baseline and Week 26, Week 52, Week 104]

Measure Type	Secondary
Measure Title	Change From Baseline in Percent of Arterial Oxygen Saturation Measured by Pulse Oximetry Before and After the 6-Minute Walk Test
Measure Description	The 6-minute walk test measured the distance participants could walk quickly on a flat, hard surface in 6 minutes. Percent (%) of arterial oxygen saturation, as measured by pulse oximetry, was to be assessed before and after the 6-minute walk test at Baseline, Week 26, Week 52 and Week 104.
Time Frame	Baseline and Week 26, Week 52, Week 104
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The FAS population consisted of all participants at selected sites who received at least one dose of study drug and had a Baseline and Week 26, Week 52 or Week 104 assessment for pre- and post-6-minute-walk-test arterial oxygen saturation. The study was terminated during Period 2; no data were collected for this endpoint at Week 104.

Reporting Groups

	Description
Navarixin 10 mg	Participants receive navarixin 10 mg, as one navarixin 10 mg capsule and two placebo capsules, administered orally QD for up to 2 years
Navarixin 30 mg	Participants receive navarixin 30 mg, as one navarixin 30 mg capsule and two placebo capsules, administered orally QD for up to 2 years
Navarixin 50 mg	Participants receive navarixin 50 mg, as two navarixin 10 mg capsules and one navarixin 30 mg capsule, administered orally QD for up to 2 years
Placebo	Participants receive placebo to navarixin, as three placebo capsules, administered orally QD for up to 2 years

Measured Values

	Navarixin 10 mg	**Navarixin 30 mg**	**Navarixin 50 mg**	**Placebo**
Number of Participants Analyzed [units: participants]	**84**	**77**	**68**	**87**
Change From Baseline in Percent of Arterial Oxygen Saturation Measured by Pulse Oximetry Before and After the 6-Minute Walk Test [units: Percent Oxygen Saturation] Least Squares Mean (Standard Error)				

Pre-walk Change at Week 26 (n=84, 77, 68, 87)	**0.12 (0.21)**	**-0.70 (0.22)**	**-0.07 (0.23)**	**-0.02 (0.21)**
Pre-walk Change at Week 52 (n=32, 25, 25, 30)	**0.19 (0.32)**	**-0.08 (0.36)**	**-0.22 (0.36)**	**-0.00 (0.33)**
Post-walk Change at Week 26 (n=84, 77, 68, 87)	**0.26 (0.32)**	**-0.42 (0.33)**	**0.28 (0.35)**	**0.75 (0.32)**
Post-walk Change at Week 52 (n=32, 25, 25, 30)	**0.39 (0.45)**	**-0.33 (0.49)**	**0.63 (0.50)**	**0.19 (0.46)**
Pre-walk Change at Week 104 (n=0, 0, 0, 0)	**NA [1]**	**NA [1]**	**NA [1]**	**NA [1]**
Post-walk Change at Week 104 (n=0, 0, 0, 0)	**NA [1]**	**NA [1]**	**NA [1]**	**NA [1]**

[1] Study terminated; data not collected.

No statistical analysis provided for Change From Baseline in Percent of Arterial Oxygen Saturation Measured by Pulse Oximetry Before and After the 6-Minute Walk Test

31. Secondary: Percentage of Participants Who Experienced an AE Related to Respiratory Infection [Time Frame: Up to 26 , 52 and 104 weeks]

Measure Type	Secondary
Measure Title	Percentage of Participants Who Experienced an AE Related to Respiratory Infection
Measure Description	The percentage of participants who experienced an AE related to a respiratory infection or infestation, was to be calculated for the first 26 weeks, the first 52 weeks and the first 104 weeks of treatment.
Time Frame	Up to 26 , 52 and 104 weeks
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The ASaT population consisted of all participants who received at least one dose of study drug. The study was terminated during Period 2; no data were analyzed for this endpoint for up to 104 weeks.

Reporting Groups

	Description
Navarixin 10 mg	Participants receive navarixin 10 mg, as one navarixin 10 mg capsule and two placebo capsules, administered orally QD for up to 2 years
Navarixin 30 mg	Participants receive navarixin 30 mg, as one navarixin 30 mg capsule and two placebo capsules, administered orally QD for up to 2 years
Navarixin 50 mg	Participants receive navarixin 50 mg, as two navarixin 10 mg capsules and one navarixin 30 mg capsule, administered orally QD for up to 2 years
Placebo	Participants receive placebo to navarixin, as three placebo capsules, administered orally QD for up to 2 years

Measured Values

	Navarixin 10 mg	**Navarixin 30 mg**	**Navarixin 50 mg**	**Placebo**

Number of Participants Analyzed [units: participants]	**152**	**156**	**152**	**154**
Percentage of Participants Who Experienced an AE Related to Respiratory Infection [units: Percentage of Participants]				
Up to Week 26 (n=152, 165, 152, 154)	**30.3**	**30.1**	**22.4**	**24.0**
Up to Week 52 (n=75, 63, 55, 82)	**41.3**	**41.3**	**38.2**	**28.0**
Up to Week 104 (n=0, 0, 0, 0)	**NA [1]**	**NA [1]**	**NA [1]**	**NA [1]**

[1] Study terminated; data not analyzed.

No statistical analysis provided for Percentage of Participants Who Experienced an AE Related to Respiratory Infection

32. Secondary: Percentage of Participants Who Experienced an AE Related to Any Type of Infection [Time Frame: Up to 26 , 52 and 104 weeks]

Measure Type	Secondary
Measure Title	Percentage of Participants Who Experienced an AE Related to Any Type of Infection
Measure Description	The percentage of participants who experienced an AE related to any type of infection or infestation, was to be calculated for the first 26 weeks, the first 52 weeks and the first 104 weeks of treatment.
Time Frame	Up to 26 , 52 and 104 weeks
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The ASaT population consisted of all participants who received at least one dose of study drug. The study was terminated during Period 2; no data were analyzed for this endpoint for up to 104 weeks.

Reporting Groups

	Description
Navarixin 10 mg	Participants receive navarixin 10 mg, as one navarixin 10 mg capsule and two placebo capsules, administered orally QD for up to 2 years
Navarixin 30 mg	Participants receive navarixin 30 mg, as one navarixin 30 mg capsule and two placebo capsules, administered orally QD for up to 2 years
Navarixin 50 mg	Participants receive navarixin 50 mg, as two navarixin 10 mg capsules and one navarixin 30 mg capsule, administered orally QD for up to 2 years
Placebo	Participants receive placebo to navarixin, as three placebo capsules, administered orally QD for up to 2 years

Measured Values

	Navarixin 10 mg	**Navarixin 30 mg**	**Navarixin 50 mg**	**Placebo**
Number of Participants Analyzed [units: participants]	**152**	**156**	**152**	**154**
Percentage of Participants Who Experienced an AE Related to Any Type				

of Infection [units: Percentage of Participants]				
Up to Week 26 (n=152, 156, 152, 154)	34.2	37.2	27.0	31.8
Up to Week 52 (n=75, 63, 55, 82)	48.0	46.0	45.5	35.4
Up to Week 104 (n=0, 0, 0, 0)	NA [1]	NA [1]	NA [1]	NA [1]

[1] Study terminated; data not analyzed.

No statistical analysis provided for Percentage of Participants Who Experienced an AE Related to Any Type of Infection

Serious Adverse Events

Hide Serious Adverse Events

Time Frame	Up to one week after last dose of study drug (up to 105 weeks)
Additional Description	The ASaT population consisted of all participants who received at least one dose of study drug.

Reporting Groups

	Description
Navarixin 10 mg	Participants receive navarixin 10 mg, as one navarixin 10 mg capsule and two placebo capsules, administered orally QD for up to 2 years
Navarixin 30 mg	Participants receive navarixin 30 mg, as one navarixin 30 mg capsule and two placebo capsules, administered orally QD for up to 2 years
Navarixin 50 mg	Participants receive navarixin 50 mg, as two navarixin 10 mg capsules and one navarixin 30 mg capsule, administered orally QD for up to 2 years
Placebo	Participants receive placebo to navarixin, as three placebo capsules, administered orally QD for up to 2 years

Serious Adverse Events

	Navarixin 10 mg	Navarixin 30 mg	Navarixin 50 mg	Placebo
Total, serious adverse events				
# participants affected / at risk	26/152 (17.11%)	23/156 (14.74%)	20/152 (13.16%)	21/154 (13.64%)
Blood and lymphatic system disorders				
Leukopenia † 1				
# participants affected / at risk	1/152 (0.66%)	0/156 (0.00%)	0/152 (0.00%)	0/154 (0.00%)
# events	1	0	0	0
Cardiac disorders				
Acute myocardial infarction † 1				
# participants affected / at risk	0/152 (0.00%)	0/156 (0.00%)	1/152 (0.66%)	0/154 (0.00%)
# events	0	0	1	0
Atrial fibrillation † 1				
# participants affected / at risk	0/152 (0.00%)	0/156 (0.00%)	1/152 (0.66%)	1/154 (0.65%)

# events	0	0	1	1
Atrial flutter † 1				
# participants affected / at risk	0/152 (0.00%)	0/156 (0.00%)	1/152 (0.66%)	0/154 (0.00%)
# events	0	0	1	0
Atrioventricular block second degree † 1				
# participants affected / at risk	1/152 (0.66%)	0/156 (0.00%)	0/152 (0.00%)	0/154 (0.00%)
# events	1	0	0	0
Cardiac failure † 1				
# participants affected / at risk	1/152 (0.66%)	0/156 (0.00%)	0/152 (0.00%)	0/154 (0.00%)
# events	1	0	0	0
Cardiac failure acute † 1				
# participants affected / at risk	0/152 (0.00%)	0/156 (0.00%)	0/152 (0.00%)	1/154 (0.65%)
# events	0	0	0	1
Cardiac failure congestive † 1				
# participants affected / at risk	0/152 (0.00%)	0/156 (0.00%)	0/152 (0.00%)	1/154 (0.65%)
# events	0	0	0	1
Mitral valve incompetence † 1				
# participants affected / at risk	0/152 (0.00%)	1/156 (0.64%)	0/152 (0.00%)	0/154 (0.00%)
# events	0	1	0	0
Myocardial infarction † 1				
# participants affected / at risk	0/152 (0.00%)	1/156 (0.64%)	1/152 (0.66%)	0/154 (0.00%)
# events	0	1	1	0
Tachycardia † 1				
# participants affected / at risk	0/152 (0.00%)	0/156 (0.00%)	1/152 (0.66%)	0/154 (0.00%)
# events	0	0	1	0
Ventricular arrhythmia † 1				
# participants affected / at risk	1/152 (0.66%)	0/156 (0.00%)	0/152 (0.00%)	0/154 (0.00%)
# events	1	0	0	0
Gastrointestinal disorders				
Abdominal pain † 1				
# participants affected / at risk	0/152 (0.00%)	1/156 (0.64%)	0/152 (0.00%)	1/154 (0.65%)
# events	0	1	0	1
Abdominal pain upper † 1				
# participants affected / at risk	0/152 (0.00%)	1/156 (0.64%)	0/152 (0.00%)	0/154 (0.00%)
# events	0	1	0	0
Anal fistula † 1				
# participants affected / at risk	0/152 (0.00%)	0/156 (0.00%)	1/152 (0.66%)	0/154 (0.00%)
# events	0	0	1	0
Colitis ischaemic † 1				
# participants affected / at risk	0/152 (0.00%)	0/156 (0.00%)	0/152 (0.00%)	1/154 (0.65%)
# events	0	0	0	1
Diarrhoea † 1				
# participants affected / at risk	0/152 (0.00%)	0/156 (0.00%)	0/152 (0.00%)	1/154 (0.65%)
# events	0	0	0	1
Diverticular perforation † 1				

# participants affected / at risk	1/152 (0.66%)	0/156 (0.00%)	1/152 (0.66%)	0/154 (0.00%)
# events	1	0	1	0
Mallory-Weiss syndrome † 1				
# participants affected / at risk	1/152 (0.66%)	0/156 (0.00%)	0/152 (0.00%)	0/154 (0.00%)
# events	1	0	0	0
Megacolon † 1				
# participants affected / at risk	1/152 (0.66%)	0/156 (0.00%)	0/152 (0.00%)	0/154 (0.00%)
# events	1	0	0	0
Oesophageal varices haemorrhage † 1				
# participants affected / at risk	1/152 (0.66%)	0/156 (0.00%)	0/152 (0.00%)	0/154 (0.00%)
# events	1	0	0	0
Pancreatitis chronic † 1				
# participants affected / at risk	0/152 (0.00%)	0/156 (0.00%)	1/152 (0.66%)	0/154 (0.00%)
# events	0	0	1	0
Small intestinal obstruction † 1				
# participants affected / at risk	0/152 (0.00%)	1/156 (0.64%)	0/152 (0.00%)	0/154 (0.00%)
# events	0	1	0	0
Umbilical hernia † 1				
# participants affected / at risk	0/152 (0.00%)	1/156 (0.64%)	0/152 (0.00%)	0/154 (0.00%)
# events	0	1	0	0
Upper gastrointestinal haemorrhage † 1				
# participants affected / at risk	1/152 (0.66%)	0/156 (0.00%)	0/152 (0.00%)	0/154 (0.00%)
# events	1	0	0	0
General disorders				
Chest pain † 1				
# participants affected / at risk	1/152 (0.66%)	2/156 (1.28%)	0/152 (0.00%)	0/154 (0.00%)
# events	1	2	0	0
Cyst † 1				
# participants affected / at risk	0/152 (0.00%)	1/156 (0.64%)	0/152 (0.00%)	0/154 (0.00%)
# events	0	1	0	0
Impaired healing † 1				
# participants affected / at risk	0/152 (0.00%)	1/156 (0.64%)	0/152 (0.00%)	0/154 (0.00%)
# events	0	1	0	0
Multi-organ failure † 1				
# participants affected / at risk	0/152 (0.00%)	0/156 (0.00%)	1/152 (0.66%)	1/154 (0.65%)
# events	0	0	1	1
Oedema peripheral † 1				
# participants affected / at risk	1/152 (0.66%)	0/156 (0.00%)	0/152 (0.00%)	0/154 (0.00%)
# events	1	0	0	0
Hepatobiliary disorders				
Cholecystitis acute † 1				
# participants affected / at risk	2/152 (1.32%)	0/156 (0.00%)	0/152 (0.00%)	0/154 (0.00%)
# events	2	0	0	0
Hepatic function abnormal † 1				
# participants affected / at risk	0/152 (0.00%)	0/156 (0.00%)	0/152 (0.00%)	1/154 (0.65%)

# events	0	0	0	1
Immune system disorders				
Anaphylactic reaction † 1				
# participants affected / at risk	1/152 (0.66%)	0/156 (0.00%)	0/152 (0.00%)	0/154 (0.00%)
# events	1	0	0	0
Infections and infestations				
Abscess † 1				
# participants affected / at risk	0/152 (0.00%)	0/156 (0.00%)	1/152 (0.66%)	0/154 (0.00%)
# events	0	0	1	0
Breast abscess † 1				
# participants affected / at risk	0/152 (0.00%)	0/156 (0.00%)	1/152 (0.66%)	0/154 (0.00%)
# events	0	0	1	0
Diverticulitis † 1				
# participants affected / at risk	1/152 (0.66%)	0/156 (0.00%)	0/152 (0.00%)	0/154 (0.00%)
# events	1	0	0	0
Infectious peritonitis † 1				
# participants affected / at risk	1/152 (0.66%)	0/156 (0.00%)	0/152 (0.00%)	0/154 (0.00%)
# events	1	0	0	0
Infectious pleural effusion † 1				
# participants affected / at risk	0/152 (0.00%)	1/156 (0.64%)	0/152 (0.00%)	0/154 (0.00%)
# events	0	2	0	0
Infective exacerbation of chronic obstructive airways disease † 1				
# participants affected / at risk	0/152 (0.00%)	1/156 (0.64%)	0/152 (0.00%)	0/154 (0.00%)
# events	0	1	0	0
Lower respiratory tract infection † 1				
# participants affected / at risk	3/152 (1.97%)	1/156 (0.64%)	0/152 (0.00%)	0/154 (0.00%)
# events	3	1	0	0
Otitis media chronic † 1				
# participants affected / at risk	0/152 (0.00%)	0/156 (0.00%)	1/152 (0.66%)	0/154 (0.00%)
# events	0	0	1	0
Pneumonia † 1				
# participants affected / at risk	2/152 (1.32%)	4/156 (2.56%)	2/152 (1.32%)	5/154 (3.25%)
# events	2	4	2	5
Scrotal abscess † 1				
# participants affected / at risk	0/152 (0.00%)	0/156 (0.00%)	1/152 (0.66%)	0/154 (0.00%)
# events	0	0	1	0
Sepsis † 1				
# participants affected / at risk	0/152 (0.00%)	0/156 (0.00%)	1/152 (0.66%)	0/154 (0.00%)
# events	0	0	1	0
Septic shock † 1				
# participants affected / at risk	0/152 (0.00%)	0/156 (0.00%)	0/152 (0.00%)	1/154 (0.65%)
# events	0	0	0	1
Injury, poisoning and procedural complications				
Contusion † 1				

# participants affected / at risk	1/152 (0.66%)	0/156 (0.00%)	0/152 (0.00%)	0/154 (0.00%)
# events	1	0	0	0
Femoral neck fracture † 1				
# participants affected / at risk	0/152 (0.00%)	1/156 (0.64%)	1/152 (0.66%)	0/154 (0.00%)
# events	0	1	1	0
Meniscus lesion † 1				
# participants affected / at risk	1/152 (0.66%)	0/156 (0.00%)	0/152 (0.00%)	0/154 (0.00%)
# events	1	0	0	0
Rib fracture † 1				
# participants affected / at risk	1/152 (0.66%)	0/156 (0.00%)	0/152 (0.00%)	1/154 (0.65%)
# events	1	0	0	1
Skull fracture † 1				
# participants affected / at risk	0/152 (0.00%)	0/156 (0.00%)	0/152 (0.00%)	1/154 (0.65%)
# events	0	0	0	1
Thoracic vertebral fracture † 1				
# participants affected / at risk	0/152 (0.00%)	1/156 (0.64%)	0/152 (0.00%)	0/154 (0.00%)
# events	0	1	0	0
Investigations				
Alanine aminotransferase increased † 1				
# participants affected / at risk	0/152 (0.00%)	0/156 (0.00%)	0/152 (0.00%)	1/154 (0.65%)
# events	0	0	0	1
Arteriogram coronary † 1				
# participants affected / at risk	0/152 (0.00%)	0/156 (0.00%)	1/152 (0.66%)	0/154 (0.00%)
# events	0	0	1	0
Aspartate aminotransferase increased † 1				
# participants affected / at risk	0/152 (0.00%)	0/156 (0.00%)	0/152 (0.00%)	1/154 (0.65%)
# events	0	0	0	1
Blood bilirubin increased † 1				
# participants affected / at risk	0/152 (0.00%)	0/156 (0.00%)	0/152 (0.00%)	1/154 (0.65%)
# events	0	0	0	1
Blood lactate dehydrogenase increased † 1				
# participants affected / at risk	0/152 (0.00%)	0/156 (0.00%)	0/152 (0.00%)	1/154 (0.65%)
# events	0	0	0	1
Blood urea increased † 1				
# participants affected / at risk	0/152 (0.00%)	0/156 (0.00%)	0/152 (0.00%)	1/154 (0.65%)
# events	0	0	0	1
Haemoglobin decreased † 1				
# participants affected / at risk	0/152 (0.00%)	0/156 (0.00%)	0/152 (0.00%)	1/154 (0.65%)
# events	0	0	0	1
Metabolism and nutrition disorders				
Diabetes mellitus inadequate control † 1				
# participants affected / at risk	1/152 (0.66%)	0/156 (0.00%)	0/152 (0.00%)	0/154 (0.00%)
# events	1	0	0	0
Musculoskeletal and connective tissue disorders				
Tenosynovitis stenosans † 1				

# participants affected / at risk	0/152 (0.00%)	0/156 (0.00%)	0/152 (0.00%)	1/154 (0.65%)
# events	0	0	0	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)				
Lung adenocarcinoma † 1				
# participants affected / at risk	1/152 (0.66%)	0/156 (0.00%)	0/152 (0.00%)	0/154 (0.00%)
# events	1	0	0	0
Non-Hodgkin's lymphoma † 1				
# participants affected / at risk	0/152 (0.00%)	0/156 (0.00%)	1/152 (0.66%)	0/154 (0.00%)
# events	0	0	1	0
Oral neoplasm † 1				
# participants affected / at risk	1/152 (0.66%)	0/156 (0.00%)	0/152 (0.00%)	0/154 (0.00%)
# events	1	0	0	0
Prostate cancer † 1				
# participants affected / at risk	1/152 (0.66%)	0/156 (0.00%)	0/152 (0.00%)	0/154 (0.00%)
# events	1	0	0	0
Renal cancer Stage IV † 1				
# participants affected / at risk	0/152 (0.00%)	0/156 (0.00%)	1/152 (0.66%)	0/154 (0.00%)
# events	0	0	1	0
Nervous system disorders				
Cerebrovascular accident † 1				
# participants affected / at risk	1/152 (0.66%)	0/156 (0.00%)	0/152 (0.00%)	0/154 (0.00%)
# events	1	0	0	0
Encephalopathy † 1				
# participants affected / at risk	0/152 (0.00%)	0/156 (0.00%)	1/152 (0.66%)	0/154 (0.00%)
# events	0	0	1	0
Facial nerve disorder † 1				
# participants affected / at risk	0/152 (0.00%)	1/156 (0.64%)	0/152 (0.00%)	0/154 (0.00%)
# events	0	1	0	0
Ischaemic stroke † 1				
# participants affected / at risk	1/152 (0.66%)	1/156 (0.64%)	0/152 (0.00%)	0/154 (0.00%)
# events	1	1	0	0
Transient ischaemic attack † 1				
# participants affected / at risk	0/152 (0.00%)	0/156 (0.00%)	1/152 (0.66%)	0/154 (0.00%)
# events	0	0	1	0
Psychiatric disorders				
Alcoholism † 1				
# participants affected / at risk	1/152 (0.66%)	0/156 (0.00%)	0/152 (0.00%)	0/154 (0.00%)
# events	1	0	0	0
Hallucination † 1				
# participants affected / at risk	0/152 (0.00%)	0/156 (0.00%)	0/152 (0.00%)	1/154 (0.65%)
# events	0	0	0	1
Renal and urinary disorders				
Renal failure acute † 1				
# participants affected / at risk	0/152 (0.00%)	1/156 (0.64%)	0/152 (0.00%)	0/154 (0.00%)

# events	0	1	0	0
Renal impairment † 1				
# participants affected / at risk	1/152 (0.66%)	0/156 (0.00%)	0/152 (0.00%)	0/154 (0.00%)
# events	1	0	0	0
Reproductive system and breast disorders				
Benign prostatic hyperplasia † 1				
# participants affected / at risk	0/152 (0.00%)	0/156 (0.00%)	0/152 (0.00%)	1/154 (0.65%)
# events	0	0	0	1
Respiratory, thoracic and mediastinal disorders				
Acute respiratory failure † 1				
# participants affected / at risk	2/152 (1.32%)	2/156 (1.28%)	0/152 (0.00%)	0/154 (0.00%)
# events	2	2	0	0
Chronic obstructive pulmonary disease † 1				
# participants affected / at risk	9/152 (5.92%)	5/156 (3.21%)	6/152 (3.95%)	4/154 (2.60%)
# events	10	6	6	10
Chronic respiratory failure † 1				
# participants affected / at risk	1/152 (0.66%)	0/156 (0.00%)	0/152 (0.00%)	0/154 (0.00%)
# events	1	0	0	0
Emphysema † 1				
# participants affected / at risk	0/152 (0.00%)	1/156 (0.64%)	0/152 (0.00%)	0/154 (0.00%)
# events	0	1	0	0
Haemoptysis † 1				
# participants affected / at risk	1/152 (0.66%)	0/156 (0.00%)	0/152 (0.00%)	0/154 (0.00%)
# events	1	0	0	0
Lung disorder † 1				
# participants affected / at risk	0/152 (0.00%)	1/156 (0.64%)	0/152 (0.00%)	1/154 (0.65%)
# events	0	1	0	1
Pulmonary cavitation † 1				
# participants affected / at risk	0/152 (0.00%)	0/156 (0.00%)	0/152 (0.00%)	1/154 (0.65%)
# events	0	0	0	1
Respiratory depression † 1				
# participants affected / at risk	1/152 (0.66%)	0/156 (0.00%)	0/152 (0.00%)	0/154 (0.00%)
# events	1	0	0	0
Respiratory failure † 1				
# participants affected / at risk	0/152 (0.00%)	0/156 (0.00%)	1/152 (0.66%)	0/154 (0.00%)
# events	0	0	1	0
Sleep apnoea syndrome † 1				
# participants affected / at risk	0/152 (0.00%)	0/156 (0.00%)	0/152 (0.00%)	1/154 (0.65%)
# events	0	0	0	1
Surgical and medical procedures				
Arterial bypass operation † 1				
# participants affected / at risk	1/152 (0.66%)	0/156 (0.00%)	0/152 (0.00%)	0/154 (0.00%)
# events	1	0	0	0
Inguinal hernia repair † 1				
# participants affected / at risk	0/152 (0.00%)	0/156 (0.00%)	1/152 (0.66%)	0/154 (0.00%)

# events	0	0	1	0
Prostatectomy † 1				
# participants affected / at risk	0/152 (0.00%)	0/156 (0.00%)	0/152 (0.00%)	1/154 (0.65%)
# events	0	0	0	1
Vascular disorders				
Arterial disorder † 1				
# participants affected / at risk	0/152 (0.00%)	1/156 (0.64%)	0/152 (0.00%)	0/154 (0.00%)
# events	0	1	0	0
Intermittent claudication † 1				
# participants affected / at risk	1/152 (0.66%)	0/156 (0.00%)	0/152 (0.00%)	0/154 (0.00%)
# events	1	0	0	0

† Events were collected by systematic assessment
1 Term from vocabulary, MedDRA 14.1

Other Adverse Events

Hide Other Adverse Events

Time Frame	Up to one week after last dose of study drug (up to 105 weeks)
Additional Description	The ASaT population consisted of all participants who received at least one dose of study drug.

Frequency Threshold

Threshold above which other adverse events are reported	5%

Reporting Groups

	Description
Navarixin 10 mg	Participants receive navarixin 10 mg, as one navarixin 10 mg capsule and two placebo capsules, administered orally QD for up to 2 years
Navarixin 30 mg	Participants receive navarixin 30 mg, as one navarixin 30 mg capsule and two placebo capsules, administered orally QD for up to 2 years
Navarixin 50 mg	Participants receive navarixin 50 mg, as two navarixin 10 mg capsules and one navarixin 30 mg capsule, administered orally QD for up to 2 years
Placebo	Participants receive placebo to navarixin, as three placebo capsules, administered orally QD for up to 2 years

Other Adverse Events

	Navarixin 10 mg	Navarixin 30 mg	Navarixin 50 mg	Placebo
Total, other (not including serious) adverse events				
# participants affected / at risk	65/152 (42.76%)	75/156 (48.08%)	74/152 (48.68%)	46/154 (29.87%)
Infections and infestations				
Influenza † 1				
# participants affected / at risk	9/152 (5.92%)	3/156 (1.92%)	4/152 (2.63%)	4/154 (2.60%)

# events	11	3	4	6
Nasopharyngitis † 1				
# participants affected / at risk	23/152 (15.13%)	28/156 (17.95%)	22/152 (14.47%)	22/154 (14.29%)
# events	38	42	34	29
Rhinitis † 1				
# participants affected / at risk	8/152 (5.26%)	6/156 (3.85%)	3/152 (1.97%)	3/154 (1.95%)
# events	8	7	3	3
Urinary tract infection † 1				
# participants affected / at risk	2/152 (1.32%)	2/156 (1.28%)	3/152 (1.97%)	8/154 (5.19%)
# events	2	2	3	11
Injury, poisoning and procedural complications				
Overdose † 1				
# participants affected / at risk	4/152 (2.63%)	4/156 (2.56%)	8/152 (5.26%)	4/154 (2.60%)
# events	5	4	9	4
Investigations				
Neutrophil count decreased † 1				
# participants affected / at risk	6/152 (3.95%)	22/156 (14.10%)	32/152 (21.05%)	1/154 (0.65%)
# events	6	22	32	1
Musculoskeletal and connective tissue disorders				
Back pain † 1				
# participants affected / at risk	10/152 (6.58%)	6/156 (3.85%)	8/152 (5.26%)	1/154 (0.65%)
# events	10	7	9	1
Nervous system disorders				
Headache † 1				
# participants affected / at risk	14/152 (9.21%)	20/156 (12.82%)	14/152 (9.21%)	15/154 (9.74%)
# events	27	29	21	22

† Events were collected by systematic assessment
1 Term from vocabulary, MedDRA 14.1

Limitations and Caveats

Hide Limitations and Caveats

Limitations of the study, such as early termination leading to small numbers of participants analyzed and technical problems with measurement leading to unreliable or uninterpretable data

No text entered.

More Information

Hide More Information

Certain Agreements:

Principal Investigators are **NOT** employed by the organization sponsoring the study.

There **IS** an agreement between Principal Investigators and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

The agreement is:

☐ The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is **less than or equal to 60 days**. The sponsor cannot require changes to the communication and cannot extend the embargo.

☐ The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is **more than 60 days but less than or equal to 180 days**. The sponsor cannot require changes to the communication and cannot extend the embargo.

Other disclosure agreement that restricts the right of the PI to discuss or publish trial results after the trial is completed.

☑ **Restriction Description:** The investigator agrees to provide to the sponsor 45 days prior to submission for publication or presentation, review copies of abstracts or manuscripts for publication (including, without limitation, slides and texts of oral or other public presentations and texts of any transmission through any electronic media, e.g., any computer access system such as the Internet, World Wide Web, etc.) that report any results of the study.

Results Point of Contact:

Name/Title: Senior Vice President, Global Clinical Development
Organization: Merck Sharp & Dohme Corp.
phone: 1-800-672-6372
e-mail: ClinicalTrialsDisclosure@merck.com

Publications of Results:

Rennard SI, Dale DC, Donohue JF, Kanniess F, Magnussen H, Sutherland ER, Watz H, Lu S, Stryszak P, Rosenberg E, Staudinger H. CXCR2 Antagonist MK-7123. A Phase 2 Proof-of-Concept Trial for Chronic Obstructive Pulmonary Disease. Am J Respir Crit Care Med. 2015 May 1;191(9):1001-11. doi: 10.1164/rccm.201405-0992OC.

Responsible Party:	Merck Sharp & Dohme Corp.
ClinicalTrials.gov Identifier:	NCT01006616 History of Changes
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Health Authority:	Canada: Health Canada

TO TOP

For Patients and Families | For Researchers | For Study Record Managers

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