ClinicalTrials.gov Protocol and Results Registration System (PRS) Receipt
Release Date: 03/02/2015

ClinicalTrials.gov ID: NCT00501046

## Study Identification

| | |
|---|---|
| Unique Protocol ID: | KRM-307 |
| Brief Title: | A Study of AST-120 for Evaluating Prevention of Progression In Chronic Kidney Disease Including Assessment of Quality of Life (EPPIC-2) |
| Official Title: | A Phase III, Randomized, Double-Blind, Placebo-Controlled Study of AST-120 for Prevention of Chronic Kidney Disease Progression in Patients With Moderate to Severe Chronic Kidney Disease Including Assessment of Quality of Life |
| Secondary IDs: | |

## Study Status

| | |
|---|---|
| Record Verification: | March 2015 |
| Overall Status: | Completed |
| Study Start: | July 2007 |
| Primary Completion: | October 2011 [Actual] |
| Study Completion: | October 2011 [Actual] |

## Sponsor/Collaborators

| | |
|---|---|
| Sponsor: | Mitsubishi Tanabe Pharma Corporation |
| Responsible Party: | Sponsor |
| Collaborators: | Kureha Corporation |

## Oversight

| | |
|---|---|
| FDA Regulated?: | Yes |

| | |
|---|---|
| Applicable Trial?: | Section 801 Clinical Trial? Yes<br>Delayed Posting? No |
| IND/IDE Protocol?: | Yes |
| IND/IDE Information: | Grantor: CDER<br>IND/IDE Number: 59,599<br>Serial Number: 034<br>Has Expanded Access? No |
| Review Board: | Approval Status:<br>Board Name:<br>Board Affiliation:<br>Phone:<br>Email: |
| Data Monitoring?: | Yes |
| Plan to Share Data?: | |
| Oversight Authorities: | United States: Food and Drug Administration<br>Russia: Ministry of Health of the Russian Federation<br>Canada: Health Canada<br>Germany: Federal Institute for Drugs and Medical Devices<br>Spain: Spanish Agency of Medicines<br>Ukraine: Ministry of Health<br>Argentina: Administracion Nacional de Medicamentos, Alimentos y Tecnologia Medica<br>Czech Republic: State Institute for Drug Control<br>Mexico: National Institute of Public Health, Health Secretariat<br>Poland: Ministry of Health<br>Brazil: National Health Surveillance Agency |

## Study Description

| | |
|---|---|
| Brief Summary: | 1) To evaluate the effectiveness of AST-120 (spherical carbon adsorbent) added to standard-of-care therapy in moderate to severe Chronic Kidney Disease (CKD), on time to first occurrence of any event of the triple composite outcome of initiation of dialysis, kidney transplant or doubling of serum creatinine (sCr) when compared with placebo; 2) To evaluate the safety and tolerability of long-term AST-120 therapy in patients with CKD; 3) To evaluate the effects of AST-120 versus placebo, on other measures of renal function and quality of life. |
| Detailed Description: | |

## Conditions

| | |
|---|---|
| Conditions: | Chronic Kidney Disease |

Keywords: Kidney Diseases

## Study Design

Study Type: Interventional
Primary Purpose: Treatment
Study Phase: Phase 3
Intervention Model: Parallel Assignment
Number of Arms: 2
Masking: Double Blind (Subject, Caregiver, Investigator, Outcomes Assessor)
Allocation: Randomized
Endpoint Classification: Safety/Efficacy Study
Enrollment: 1015 [Actual]

## Arms and Interventions

| Arms | Assigned Interventions |
|---|---|
| Placebo Comparator: Placebo | Drug: Placebo<br>9g /day (3 times a day) |
| Experimental: AST-120 | Drug: AST-120<br>9g /day (3 times a day) |

## Outcome Measures

[See Results Section.]

## Eligibility

Minimum Age: 18 Years
Maximum Age:
Gender: Both
Accepts Healthy Volunteers?: No
Criteria: Inclusion Criteria:

- Age 18 years or older
- Moderate to severe CKD, not anticipated to require dialysis or renal transplant within the next 6 months

- Patient survival expected to be no less than one year
- Serum creatinine in men >= 2.0 mg/dL (>= 177 µmol/L) and <= 5.0 mg/dL (<= 442 µmol/L), and in women >= 1.5 mg/dL (>= 133 µmol/L) and <= 5.0 mg/dL (<= 442 µmol/L) at Screening
- Urinary total protein to urinary total creatinine ratio must be >= 0.5 on a spot void obtained at Screening
- Blood pressure <= 160/90 mmHg at both Screening and Baseline visits. In addition, blood pressure, if measured, must have been stable in hypertensive patients over the 3 months prior to Screening, with no more than 1 blood pressure reading > 160/90 mmHg
- In patients being treated for hypertension, they should be on a stable anti-hypertensive regimen

Exclusion Criteria:

- Obstructive or reversible cause of kidney disease
- Nephrotic syndrome defined as a ratio of urinary total protein to urinary creatinine of > 6.0 as measured on a spot void
- Adult polycystic kidney disease
- History of previous kidney transplant
- History of recent (within the past 6 months) accelerated or malignant hypertension
- Uncontrolled arrhythmia or severe cardiac disease within the past 6 months
- History of malabsorption, inflammatory bowel disease, hiatal hernia, active peptic ulcer, or severe GI dysmotility, not attributable to the use of a phosphate binder
- Received any investigational agent or participated in a clinical study within the previous 3 months
- Presence of any significant medical condition that might create an undue risk with study participation, or significantly confound the collection of safety and efficacy data in this study

## Contacts/Locations

Study Officials: Professor
Study Principal Investigator
Information at Mitsubishi Tanabe Pharma Development America, Inc.

Locations: United States, Alabama
Tuscaloosa, Alabama, United States

United States, Arkansas
Hot Springs, Arkansas, United States

United States, California
Bakersfield, California, United States

United States, Florida
West Palm Beach, Florida, United States

United States, Georgia
Augusta, Georgia, United States

United States, Hawaii

Honolulu, Hawaii, United States

United States, Michigan
Pontiac, Michigan, United States

United States, Minnesota
Brooklyn Center, Minnesota, United States

United States, North Carolina
Elizabeth City, North Carolina, United States

United States, New York
Flushing, New York, United States

United States, Pennsylvania
Allentown, Pennsylvania, United States

Doylestown, Pennsylvania, United States

Lancaster, Pennsylvania, United States

Puerto Rico
San Juan, Puerto Rico

United States, Tennessee
Knoxville, Tennessee, United States

United States, Texas
Houston, Texas, United States

United States, Virginia
Fairfax, Virginia, United States

United States, Washington
Vancouver, Washington, United States

United States, South Carolina
Orangeburg, South Carolina, United States

United States, Tennessee
Nashville, Tennessee, United States

United States, California
Glendale, California, United States

Riverside, California, United States

United States, South Carolina
Sumter, South Carolina, United States

United States, Colorado
Denver, Colorado, United States

United States, Louisiana
Kenner, Louisiana, United States

Russian Federation
Arkhangelsk, Russian Federation

Moscow, Russian Federation

Petrozavodsk, Russian Federation

Saratov, Russian Federation

St. Petersburg, Russian Federation

United States, Louisiana
Shreveport, Louisiana, United States

United States, Ohio
Cincinnati, Ohio, United States

United States, Virginia
Richmond, Virginia, United States

United States, Wisconsin
Milwaukee, Wisconsin, United States

Germany
Hamburg, Germany

Kiel, Germany

Mainz, Germany

Canada, Quebec
Greenfield Park, Quebec, Canada

Russian Federation
Kemerovo, Russian Federation

Novosibirsk, Russian Federation

Ukraine
Ivano-Frankivsk, Ukraine

Kharkov, Ukraine

Kiev, Ukraine

Nikolaev, Ukraine

Ternopol, Ukraine

Zaporizhzhya, Ukraine

United States, South Carolina
Charleston, South Carolina, United States

United States, California
Los Angeles, California, United States

Palo Alto, California, United States

Argentina
Buenos Aires, Argentina

Cordoba, Argentina

Canada, British Columbia
Vancouver, British Columbia, Canada

Canada, Quebec
Montreal, Quebec, Canada

Czech Republic
Hradec Kralove, Czech Republic

Liberec, Czech Republic

Praha, Czech Republic

Usti nad Labem, Czech Republic

Mexico
Aguascalientes, Mexico

Cuernavaca, Mexico

Mexico City, Mexico

Poland
Bialystok, Poland

Czestochowa, Poland

Warszawa, Poland

United States, Texas
Dallas, Texas, United States

Spain
Madrid, Spain

Asturias, Spain

Barcelona, Spain

Guadalajara, Spain

Canada, Alberta
Calgary, Alberta, Canada

United States, Rhode Island
Providence, Rhode Island, United States

Argentina
Tucumán, Argentina

Poland
Lublin, Poland

United States, Florida
Boynton Beach, Florida, United States

United States, Georgia
Macon, Georgia, United States

United States, Illinois
Evergreen Park, Illinois, United States

United States, Kansas
Shawnee, Kansas, United States

United States, New York
New York, New York, United States

Great Neck, New York, United States

Williamsville, New York, United States

United States, Oregon
Bend, Oregon, United States

United States, South Carolina
Columbia, South Carolina, United States

United States, Virginia
Arlington, Virginia, United States

Norfolk, Virginia, United States

Suffolk, Virginia, United States

United States, West Virginia
Morgantown, West Virginia, United States

Brazil
Belo Horizonte, Brazil

Botucatu, Brazil

Campinas, Brazil

Curitiba, Brazil

Ibirapuera, Brazil

Porto Alegre, Brazil

Rio de Janeiro, Brazil

São Paulo, Brazil

Mexico
Durango, Mexico

Russian Federation
Ekaterinburg, Russian Federation

Orenburg, Russian Federation

Tomsk, Russian Federation

Yaroslayl, Russian Federation

Spain
A Coruña, Spain

Ukraine
Lugansk, Ukraine

Lviv, Ukraine

Poltava, Ukraine

Vinnitsa, Ukraine

Brazil
Sorocaba, Brazil

Mexico
Mexico, Mexico

Russian Federation
Chelyabinsk, Russian Federation

## References

Citations: [Study Results] Schulman G, Berl T, Beck GJ, Remuzzi G, Ritz E, Arita K, Kato A, Shimizu M. Randomized Placebo-Controlled EPPIC Trials of AST-120 in CKD. J Am Soc Nephrol. 2015 Jul;26(7):1732-46. doi: 10.1681/ASN.2014010042. Epub 2014 Oct 27. PubMed 25349205

Links:

Study Data/Documents:

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# Study Results

## Participant Flow

Reporting Groups

| | Description |
|---|---|
| AST-120 | AST-120: 9g /day (3 times a day) |
| Placebo | Placebo: 9g /day (3 times a day) |

Overall Study

| | AST-120 | Placebo |
|---|---|---|
| Started | 508 | 507 |
| Completed | 238 | 213 |
| Not Completed | 270 | 294 |
| Adverse Event | 21 | 25 |
| Death | 23 | 30 |
| Lost to Follow-up | 14 | 13 |
| Physician Decision | 7 | 2 |
| Pregnancy | 0 | 3 |
| Protocol Violation | 2 | 1 |
| Withdrawal by Subject | 84 | 83 |
| Reaching endpoints,Noncompliance,etc | 119 | 137 |

## Baseline Characteristics

Reporting Groups

| | Description |
|---|---|
| AST-120 | AST-120: 9g /day (3 times a day) |
| Placebo | Placebo: 9g /day (3 times a day) |

Baseline Measures

| | AST-120 | Placebo | Total |
|---|---|---|---|
| Number of Participants | 508 | 507 | 1015 |
| Age, Continuous<br>[units: years]<br>Mean (Standard Deviation) | 54.4 (15.52) | 55.7 (14.66) | 55.1 (15.11) |
| Gender, Male/Female<br>[units: participants] | | | |
| Female | 229 | 226 | 455 |
| Male | 279 | 281 | 560 |

## Outcome Measures

1. Primary Outcome Measure:

| | |
|---|---|
| Measure Title | Composite of Dialysis Initiation, Kidney Transplantation, and Serum Creatinine Doubling. Number of Participants Meeting the Criteria Are Reported. |
| Measure Description | |
| Time Frame | Beyond Week 48, a 12-week visit cycle continued until the end of the study or until individual patients reached an endpoint |
| Safety Issue? | No |

Analysis Population Description
ITT (censored at last contact)

Reporting Groups

| | Description |
|---|---|
| AST-120 | AST-120: 9g /day (3 times a day) |
| Placebo | Placebo: 9g /day (3 times a day) |

Measured Values

| | AST-120 | Placebo |
|---|---|---|
| Number of Participants Analyzed | 500 | 497 |
| Composite of Dialysis Initiation, Kidney Transplantation, and Serum Creatinine Doubling. Number of Participants Meeting the Criteria Are Reported. [units: participants] | 172 | 183 |

2. Primary Outcome Measure:

| | |
|---|---|
| Measure Title | Safety and Tolerability |
| Measure Description | |
| Time Frame | approximately 42 months |
| Safety Issue? | Yes |

Outcome Measure Data Not Reported

3. Secondary Outcome Measure:

| | |
|---|---|
| Measure Title | The Development of a Component of a Quadruple Composite Endpoint (Initiation of Dialysis, Kidney Transplant, Doubling of sCr, or Death), Other Measures of Renal Function and (QOL: Exploratory) |
| Measure Description | |
| Time Frame | approximately 42 months |
| Safety Issue? | No |

Outcome Measure Data Not Reported

4. Secondary Outcome Measure:

| | |
|---|---|
| Measure Title | Vitamins and Folate Levels |
| Measure Description | |
| Time Frame | approximately 42 months |
| Safety Issue? | Yes |

Outcome Measure Data Not Reported

## Reported Adverse Events

| | |
|---|---|
| Time Frame | [Not specified] |
| Additional Description | The AE analysis is based on the Safety Population. The Safety Population included all patients who were randomized and received at least 1 dose of study drug. The start number of Participant Flow included all patients who were randomized. |

Reporting Groups

| | Description |
|---|---|
| AST-120 | AST-120: 9g /day (3 times a day) |
| Placebo | Placebo: 9g /day (3 times a day) |

Serious Adverse Events

| | AST-120 | Placebo |
|---|---|---|
| | Affected/At Risk (%) | Affected/At Risk (%) |
| Total | 156/507 (30.77%) | 178/505 (35.25%) |
| Blood and lymphatic system disorders | | |

| | AST-120 | Placebo |
|---|---|---|
| | Affected/At Risk (%) | Affected/At Risk (%) |
| Anaemia | 7/507 (1.38%) | 6/505 (1.19%) |
| Haemolytic anaemia | 1/507 (0.2%) | 0/505 (0%) |
| Iron deficiency anaemia | 0/507 (0%) | 1/505 (0.2%) |
| Cardiac disorders | | |
| Acute coronary syndrome | 2/507 (0.39%) | 0/505 (0%) |
| Acute left ventricular failure | 1/507 (0.2%) | 0/505 (0%) |
| Acute myocardial infarction | 8/507 (1.58%) | 6/505 (1.19%) |
| Angina pectoris | 2/507 (0.39%) | 5/505 (0.99%) |
| Angina unstable | 5/507 (0.99%) | 4/505 (0.79%) |
| Arrhythmia | 1/507 (0.2%) | 0/505 (0%) |
| Arteriosclerosis coronary artery | 1/507 (0.2%) | 2/505 (0.4%) |
| Atrial fibrillation | 4/507 (0.79%) | 1/505 (0.2%) |
| Atrial flutter | 2/507 (0.39%) | 1/505 (0.2%) |
| Atrioventricular block | 1/507 (0.2%) | 0/505 (0%) |
| Atrioventricular block complete | 1/507 (0.2%) | 0/505 (0%) |
| Atrioventricular block first degree | 2/507 (0.39%) | 0/505 (0%) |
| Atrioventricular block second degree | 0/507 (0%) | 1/505 (0.2%) |
| Bradycardia | 1/507 (0.2%) | 4/505 (0.79%) |
| Cardiac arrest | 3/507 (0.59%) | 3/505 (0.59%) |
| Cardiac failure | 4/507 (0.79%) | 4/505 (0.79%) |
| Cardiac failure acute | 1/507 (0.2%) | 0/505 (0%) |
| Cardiac failure chronic | 0/507 (0%) | 1/505 (0.2%) |
| Cardiac failure congestive | 5/507 (0.99%) | 11/505 (2.18%) |
| Cardiogenic shock | 0/507 (0%) | 2/505 (0.4%) |
| Cardiomyopathy | 1/507 (0.2%) | 0/505 (0%) |
| Cardiomyopathy alcoholic | 1/507 (0.2%) | 0/505 (0%) |

| | AST-120 | Placebo |
|---|---|---|
| | Affected/At Risk (%) | Affected/At Risk (%) |
| Cardiopulmonary failure | 1/507 (0.2%) | 0/505 (0%) |
| Coronary artery disease | 3/507 (0.59%) | 3/505 (0.59%) |
| Coronary artery insufficiency | 0/507 (0%) | 1/505 (0.2%) |
| Ischaemic cardiomyopathy | 1/507 (0.2%) | 0/505 (0%) |
| Left ventricular dysfunction | 1/507 (0.2%) | 0/505 (0%) |
| Myocardial infarction | 1/507 (0.2%) | 4/505 (0.79%) |
| Myocardial ischaemia | 0/507 (0%) | 1/505 (0.2%) |
| Silent myocardial infarction | 1/507 (0.2%) | 0/505 (0%) |
| Sinus bradycardia | 1/507 (0.2%) | 1/505 (0.2%) |
| Tachycardia | 1/507 (0.2%) | 0/505 (0%) |
| Ventricular fibrillation | 1/507 (0.2%) | 1/505 (0.2%) |
| Endocrine disorders | | |
| Hyperparathyroidism tertiary | 0/507 (0%) | 1/505 (0.2%) |
| Myxoedema | 0/507 (0%) | 1/505 (0.2%) |
| Eye disorders | | |
| Cataract | 1/507 (0.2%) | 0/505 (0%) |
| Diabetic retinopathy | 1/507 (0.2%) | 0/505 (0%) |
| Gastrointestinal disorders | | |
| Abdominal hernia | 1/507 (0.2%) | 0/505 (0%) |
| Abdominal pain | 1/507 (0.2%) | 1/505 (0.2%) |
| Abdominal pain upper | 1/507 (0.2%) | 0/505 (0%) |
| Diarrhoea | 0/507 (0%) | 2/505 (0.4%) |
| Diverticular perforation | 1/507 (0.2%) | 0/505 (0%) |
| Diverticulum | 2/507 (0.39%) | 0/505 (0%) |
| Duodenal ulcer | 1/507 (0.2%) | 2/505 (0.4%) |
| Duodenitis | 1/507 (0.2%) | 1/505 (0.2%) |

| | AST-120 | Placebo |
|---|---|---|
| | Affected/At Risk (%) | Affected/At Risk (%) |
| Enterocolitis haemorrhagic | 1/507 (0.2%) | 0/505 (0%) |
| Erosive oesophagitis | 1/507 (0.2%) | 0/505 (0%) |
| Gastric ulcer | 0/507 (0%) | 1/505 (0.2%) |
| Gastritis | 3/507 (0.59%) | 4/505 (0.79%) |
| Gastritis erosive | 1/507 (0.2%) | 1/505 (0.2%) |
| Gastritis haemorrhagic | 0/507 (0%) | 1/505 (0.2%) |
| Gastrointestinal haemorrhage | 2/507 (0.39%) | 0/505 (0%) |
| Impaired gastric emptying | 1/507 (0.2%) | 0/505 (0%) |
| Intestinal obstruction | 2/507 (0.39%) | 1/505 (0.2%) |
| Large intestine perforation | 0/507 (0%) | 1/505 (0.2%) |
| Megacolon | 2/507 (0.39%) | 0/505 (0%) |
| Mouth ulceration | 0/507 (0%) | 1/505 (0.2%) |
| Nausea | 0/507 (0%) | 2/505 (0.4%) |
| Pancreatic cyst | 1/507 (0.2%) | 0/505 (0%) |
| Pancreatitis | 1/507 (0.2%) | 0/505 (0%) |
| Pancreatitis acute | 1/507 (0.2%) | 0/505 (0%) |
| Pancreatitis chronic | 0/507 (0%) | 1/505 (0.2%) |
| Peptic ulcer | 0/507 (0%) | 1/505 (0.2%) |
| Small intestinal obstruction | 1/507 (0.2%) | 0/505 (0%) |
| Upper gastrointestinal haemorrhage | 0/507 (0%) | 1/505 (0.2%) |
| Vomiting | 0/507 (0%) | 2/505 (0.4%) |
| General disorders | | |
| Asthenia | 1/507 (0.2%) | 0/505 (0%) |
| Chest pain | 0/507 (0%) | 1/505 (0.2%) |
| Death | 0/507 (0%) | 1/505 (0.2%) |
| Device difficult to use | 0/507 (0%) | 1/505 (0.2%) |

| | AST-120 | Placebo |
|---|---|---|
| | Affected/At Risk (%) | Affected/At Risk (%) |
| Device dislocation | 0/507 (0%) | 1/505 (0.2%) |
| Device lead damage | 1/507 (0.2%) | 0/505 (0%) |
| Generalised oedema | 1/507 (0.2%) | 0/505 (0%) |
| Multi-organ failure | 1/507 (0.2%) | 0/505 (0%) |
| Necrobiosis | 0/507 (0%) | 1/505 (0.2%) |
| Non-cardiac chest pain | 2/507 (0.39%) | 2/505 (0.4%) |
| Oedema | 1/507 (0.2%) | 0/505 (0%) |
| Oedema due to renal disease | 0/507 (0%) | 1/505 (0.2%) |
| Oedema peripheral | 1/507 (0.2%) | 0/505 (0%) |
| Pyrexia | 0/507 (0%) | 2/505 (0.4%) |
| Sudden cardiac death | 2/507 (0.39%) | 0/505 (0%) |
| Sudden death | 0/507 (0%) | 4/505 (0.79%) |
| Hepatobiliary disorders | | |
| Cholangitis | 1/507 (0.2%) | 0/505 (0%) |
| Cholecystitis | 1/507 (0.2%) | 0/505 (0%) |
| Cholelithiasis | 0/507 (0%) | 1/505 (0.2%) |
| Cholestasis | 1/507 (0.2%) | 0/505 (0%) |
| Infections and infestations | | |
| Abscess limb | 1/507 (0.2%) | 0/505 (0%) |
| Appendicitis | 0/507 (0%) | 1/505 (0.2%) |
| Arteriovenous fistula site infection | 1/507 (0.2%) | 1/505 (0.2%) |
| Arthritis bacterial | 1/507 (0.2%) | 0/505 (0%) |
| Bacteraemia | 1/507 (0.2%) | 0/505 (0%) |
| Bronchitis | 1/507 (0.2%) | 4/505 (0.79%) |
| Bronchitis bacterial | 1/507 (0.2%) | 0/505 (0%) |
| Cellulitis | 4/507 (0.79%) | 0/505 (0%) |

| | AST-120 | Placebo |
|---|---|---|
| | Affected/At Risk (%) | Affected/At Risk (%) |
| Cholecystitis infective | 1/507 (0.2%) | 0/505 (0%) |
| Clostridium difficile colitis | 1/507 (0.2%) | 0/505 (0%) |
| Cystitis | 1/507 (0.2%) | 0/505 (0%) |
| Diabetic gangrene | 0/507 (0%) | 1/505 (0.2%) |
| Diverticulitis | 1/507 (0.2%) | 1/505 (0.2%) |
| Enterobacter sepsis | 1/507 (0.2%) | 0/505 (0%) |
| Erysipelas | 0/507 (0%) | 2/505 (0.4%) |
| Escherichia urinary tract infection | 2/507 (0.39%) | 1/505 (0.2%) |
| Gastroenteritis | 2/507 (0.39%) | 2/505 (0.4%) |
| Gastroenteritis viral | 0/507 (0%) | 1/505 (0.2%) |
| Lobar pneumonia | 2/507 (0.39%) | 2/505 (0.4%) |
| Myringitis bullous | 1/507 (0.2%) | 0/505 (0%) |
| Osteomyelitis | 1/507 (0.2%) | 0/505 (0%) |
| Pneumonia | 10/507 (1.97%) | 4/505 (0.79%) |
| Pneumonia bacterial | 1/507 (0.2%) | 0/505 (0%) |
| Pneumonia klebsiella | 0/507 (0%) | 1/505 (0.2%) |
| Post procedural infection | 1/507 (0.2%) | 0/505 (0%) |
| Pyelonephritis | 0/507 (0%) | 2/505 (0.4%) |
| Pyelonephritis chronic | 0/507 (0%) | 1/505 (0.2%) |
| Sepsis | 5/507 (0.99%) | 3/505 (0.59%) |
| Septic shock | 2/507 (0.39%) | 2/505 (0.4%) |
| Staphylococcal infection | 0/507 (0%) | 1/505 (0.2%) |
| Streptococcal bacteraemia | 0/507 (0%) | 1/505 (0.2%) |
| Subcutaneous abscess | 1/507 (0.2%) | 1/505 (0.2%) |
| Tooth abscess | 0/507 (0%) | 1/505 (0.2%) |
| Urinary tract infection | 4/507 (0.79%) | 6/505 (1.19%) |

| | AST-120 | Placebo |
|---|---|---|
| | Affected/At Risk (%) | Affected/At Risk (%) |
| Urosepsis | 2/507 (0.39%) | 0/505 (0%) |
| Injury, poisoning and procedural complications | | |
| Accidental overdose | 1/507 (0.2%) | 0/505 (0%) |
| Arteriovenous fistula thrombosis | 0/507 (0%) | 1/505 (0.2%) |
| Fall | 1/507 (0.2%) | 0/505 (0%) |
| Femur fracture | 0/507 (0%) | 1/505 (0.2%) |
| Gastrointestinal stoma complication | 1/507 (0.2%) | 0/505 (0%) |
| Hand fracture | 0/507 (0%) | 1/505 (0.2%) |
| Post procedural myocardial infarction | 1/507 (0.2%) | 0/505 (0%) |
| Postoperative ileus | 1/507 (0.2%) | 0/505 (0%) |
| Splenic rupture | 0/507 (0%) | 1/505 (0.2%) |
| Subdural haematoma | 0/507 (0%) | 1/505 (0.2%) |
| Synovial rupture | 0/507 (0%) | 1/505 (0.2%) |
| Thermal burn | 1/507 (0.2%) | 0/505 (0%) |
| Ulna fracture | 0/507 (0%) | 1/505 (0.2%) |
| Upper limb fracture | 1/507 (0.2%) | 0/505 (0%) |
| Vascular access complication | 0/507 (0%) | 1/505 (0.2%) |
| Investigations | | |
| Chest X-ray abnormal | 1/507 (0.2%) | 0/505 (0%) |
| Electrocardiogram QRS complex prolonged | 0/507 (0%) | 1/505 (0.2%) |
| Haemoglobin decreased | 1/507 (0.2%) | 0/505 (0%) |
| Metabolism and nutrition disorders | | |
| Dehydration | 3/507 (0.59%) | 3/505 (0.59%) |
| Diabetes mellitus | 1/507 (0.2%) | 2/505 (0.4%) |
| Diabetes mellitus inadequate control | 1/507 (0.2%) | 3/505 (0.59%) |
| Diabetic foot | 1/507 (0.2%) | 2/505 (0.4%) |

| | AST-120 | Placebo |
|---|---|---|
| | Affected/At Risk (%) | Affected/At Risk (%) |
| Diabetic ketoacidosis | 3/507 (0.59%) | 0/505 (0%) |
| Electrolyte imbalance | 1/507 (0.2%) | 0/505 (0%) |
| Fluid overload | 0/507 (0%) | 2/505 (0.4%) |
| Gout | 0/507 (0%) | 2/505 (0.4%) |
| Hypercalcaemia | 1/507 (0.2%) | 1/505 (0.2%) |
| Hyperglycaemia | 3/507 (0.59%) | 2/505 (0.4%) |
| Hyperkalaemia | 4/507 (0.79%) | 4/505 (0.79%) |
| Hypoglycaemia | 1/507 (0.2%) | 5/505 (0.99%) |
| Hypokalaemia | 1/507 (0.2%) | 3/505 (0.59%) |
| Hyponatraemia | 1/507 (0.2%) | 0/505 (0%) |
| Hypovolaemia | 1/507 (0.2%) | 1/505 (0.2%) |
| Metabolic acidosis | 1/507 (0.2%) | 0/505 (0%) |
| Musculoskeletal and connective tissue disorders | | |
| Arthralgia | 1/507 (0.2%) | 0/505 (0%) |
| Arthritis | 1/507 (0.2%) | 0/505 (0%) |
| Bursitis | 0/507 (0%) | 1/505 (0.2%) |
| Gouty arthritis | 0/507 (0%) | 1/505 (0.2%) |
| Intervertebral disc protrusion | 1/507 (0.2%) | 0/505 (0%) |
| Muscular weakness | 1/507 (0.2%) | 0/505 (0%) |
| Musculoskeletal pain | 0/507 (0%) | 1/505 (0.2%) |
| Myalgia | 1/507 (0.2%) | 0/505 (0%) |
| Osteoarthritis | 0/507 (0%) | 1/505 (0.2%) |
| Osteochondritis | 1/507 (0.2%) | 0/505 (0%) |
| Rhabdomyolysis | 0/507 (0%) | 1/505 (0.2%) |
| Rotator cuff syndrome | 1/507 (0.2%) | 0/505 (0%) |
| Spinal column stenosis | 1/507 (0.2%) | 0/505 (0%) |

| | AST-120 | Placebo |
|---|---|---|
| | Affected/At Risk (%) | Affected/At Risk (%) |
| Spinal osteoarthritis | 0/507 (0%) | 1/505 (0.2%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | |
| Bladder cancer | 1/507 (0.2%) | 0/505 (0%) |
| Cardiac myxoma | 0/507 (0%) | 1/505 (0.2%) |
| Colon cancer | 1/507 (0.2%) | 0/505 (0%) |
| Endometrial cancer | 1/507 (0.2%) | 0/505 (0%) |
| Gastrointestinal tract adenoma | 0/507 (0%) | 1/505 (0.2%) |
| Lung neoplasm malignant | 0/507 (0%) | 1/505 (0.2%) |
| Metastases to liver | 1/507 (0.2%) | 0/505 (0%) |
| Metastases to peritoneum | 1/507 (0.2%) | 0/505 (0%) |
| Parathyroid tumour benign | 0/507 (0%) | 1/505 (0.2%) |
| Renal cell carcinoma | 0/507 (0%) | 1/505 (0.2%) |
| Small cell lung cancer stage unspecified | 1/507 (0.2%) | 0/505 (0%) |
| Squamous cell carcinoma of skin | 1/507 (0.2%) | 0/505 (0%) |
| Nervous system disorders | | |
| Autonomic neuropathy | 0/507 (0%) | 1/505 (0.2%) |
| Cerebral circulatory failure | 0/507 (0%) | 1/505 (0.2%) |
| Cerebral haemorrhage | 0/507 (0%) | 1/505 (0.2%) |
| Cerebral infarction | 1/507 (0.2%) | 0/505 (0%) |
| Cerebral ischaemia | 1/507 (0.2%) | 0/505 (0%) |
| Cerebrovascular accident | 7/507 (1.38%) | 5/505 (0.99%) |
| Convulsion | 1/507 (0.2%) | 1/505 (0.2%) |
| Encephalomyelitis | 1/507 (0.2%) | 0/505 (0%) |
| Encephalopathy | 0/507 (0%) | 1/505 (0.2%) |
| Haemorrhage intracranial | 1/507 (0.2%) | 1/505 (0.2%) |
| Haemorrhagic stroke | 1/507 (0.2%) | 1/505 (0.2%) |

| | AST-120 | Placebo |
|---|---|---|
| | Affected/At Risk (%) | Affected/At Risk (%) |
| Hepatic encephalopathy | 1/507 (0.2%) | 0/505 (0%) |
| Hypoglycaemic coma | 0/507 (0%) | 2/505 (0.4%) |
| Hypoglycaemic unconsciousness | 0/507 (0%) | 1/505 (0.2%) |
| Ischaemic cerebral infarction | 0/507 (0%) | 1/505 (0.2%) |
| Ischaemic stroke | 1/507 (0.2%) | 1/505 (0.2%) |
| Loss of consciousness | 1/507 (0.2%) | 0/505 (0%) |
| Polyneuropathy | 0/507 (0%) | 1/505 (0.2%) |
| Presyncope | 1/507 (0.2%) | 0/505 (0%) |
| Radiculitis lumbosacral | 0/507 (0%) | 1/505 (0.2%) |
| Syncope | 3/507 (0.59%) | 2/505 (0.4%) |
| Transient ischaemic attack | 2/507 (0.39%) | 0/505 (0%) |
| Psychiatric disorders | | |
| Delirium | 0/507 (0%) | 1/505 (0.2%) |
| Depression | 1/507 (0.2%) | 0/505 (0%) |
| Mental status changes | 2/507 (0.39%) | 0/505 (0%) |
| Renal and urinary disorders | | |
| Azotaemia | 5/507 (0.99%) | 4/505 (0.79%) |
| Calculus ureteric | 0/507 (0%) | 1/505 (0.2%) |
| Diabetic nephropathy | 1/507 (0.2%) | 1/505 (0.2%) |
| Glomerulonephritis acute | 0/507 (0%) | 1/505 (0.2%) |
| Glomerulonephritis chronic | 0/507 (0%) | 2/505 (0.4%) |
| Haematuria | 0/507 (0%) | 2/505 (0.4%) |
| Hydronephrosis | 1/507 (0.2%) | 0/505 (0%) |
| Nephrotic syndrome | 0/507 (0%) | 1/505 (0.2%) |
| Oliguria | 1/507 (0.2%) | 0/505 (0%) |
| Renal failure | 3/507 (0.59%) | 2/505 (0.4%) |

| | AST-120 | Placebo |
|---|---|---|
| | Affected/At Risk (%) | Affected/At Risk (%) |
| Renal failure acute | 14/507 (2.76%) | 13/505 (2.57%) |
| Renal failure chronic | 34/507 (6.71%) | 47/505 (9.31%) |
| Renal impairment | 0/507 (0%) | 4/505 (0.79%) |
| Urinary retention | 0/507 (0%) | 2/505 (0.4%) |
| Reproductive system and breast disorders | | |
| Benign prostatic hyperplasia | 1/507 (0.2%) | 1/505 (0.2%) |
| Dysfunctional uterine bleeding | 1/507 (0.2%) | 0/505 (0%) |
| Ovarian cyst | 1/507 (0.2%) | 1/505 (0.2%) |
| Respiratory, thoracic and mediastinal disorders | | |
| Acute pulmonary oedema | 2/507 (0.39%) | 0/505 (0%) |
| Acute respiratory failure | 1/507 (0.2%) | 0/505 (0%) |
| Atelectasis | 0/507 (0%) | 1/505 (0.2%) |
| Bronchitis chronic | 0/507 (0%) | 1/505 (0.2%) |
| Bronchospasm | 1/507 (0.2%) | 0/505 (0%) |
| Chronic obstructive pulmonary disease | 4/507 (0.79%) | 0/505 (0%) |
| Epistaxis | 1/507 (0.2%) | 0/505 (0%) |
| Hypoxia | 0/507 (0%) | 1/505 (0.2%) |
| Pleural effusion | 0/507 (0%) | 1/505 (0.2%) |
| Pulmonary congestion | 1/507 (0.2%) | 1/505 (0.2%) |
| Pulmonary hypertension | 0/507 (0%) | 1/505 (0.2%) |
| Pulmonary oedema | 1/507 (0.2%) | 2/505 (0.4%) |
| Respiratory failure | 1/507 (0.2%) | 1/505 (0.2%) |
| Skin and subcutaneous tissue disorders | | |
| Leukocytoclastic vasculitis | 0/507 (0%) | 1/505 (0.2%) |
| Rash pruritic | 1/507 (0.2%) | 0/505 (0%) |
| Skin ulcer | 1/507 (0.2%) | 0/505 (0%) |

| | AST-120 | Placebo |
|---|---|---|
| | Affected/At Risk (%) | Affected/At Risk (%) |
| Surgical and medical procedures | | |
| Arteriovenous fistula operation | 9/507 (1.78%) | 11/505 (2.18%) |
| Catheter placement | 0/507 (0%) | 1/505 (0.2%) |
| Central venous catheterisation | 0/507 (0%) | 1/505 (0.2%) |
| Cholecystectomy | 0/507 (0%) | 1/505 (0.2%) |
| Dialysis device insertion | 0/507 (0%) | 1/505 (0.2%) |
| Insertion of ambulatory peritoneal catheter | 2/507 (0.39%) | 4/505 (0.79%) |
| Obesity surgery | 0/507 (0%) | 1/505 (0.2%) |
| Vascular disorders | | |
| Aortic aneurysm rupture | 0/507 (0%) | 1/505 (0.2%) |
| Aortic stenosis | 0/507 (0%) | 1/505 (0.2%) |
| Deep vein thrombosis | 0/507 (0%) | 2/505 (0.4%) |
| Haematoma | 1/507 (0.2%) | 0/505 (0%) |
| Haemodynamic instability | 1/507 (0.2%) | 0/505 (0%) |
| Hypertension | 6/507 (1.18%) | 8/505 (1.58%) |
| Hypertensive crisis | 3/507 (0.59%) | 4/505 (0.79%) |
| Hypertensive emergency | 1/507 (0.2%) | 1/505 (0.2%) |
| Hypotension | 2/507 (0.39%) | 0/505 (0%) |
| Hypovolaemic shock | 0/507 (0%) | 2/505 (0.4%) |
| Ischaemia | 0/507 (0%) | 1/505 (0.2%) |
| Orthostatic hypotension | 1/507 (0.2%) | 0/505 (0%) |
| Peripheral ischaemia | 1/507 (0.2%) | 0/505 (0%) |
| Peripheral vascular disorder | 2/507 (0.39%) | 0/505 (0%) |
| Thrombosis | 1/507 (0.2%) | 0/505 (0%) |

Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 1%

| | AST-120 | Placebo |
|---|---|---|
| | Affected/At Risk (%) | Affected/At Risk (%) |
| Total | 393/507 (77.51%) | 377/505 (74.65%) |
| Blood and lymphatic system disorders | | |
| Anaemia | 75/507 (14.79%) | 83/505 (16.44%) |
| Cardiac disorders | | |
| Angina pectoris | 1/507 (0.2%) | 7/505 (1.39%) |
| Ear and labyrinth disorders | | |
| Vertigo | 2/507 (0.39%) | 6/505 (1.19%) |
| Endocrine disorders | | |
| Hyperparathyroidism | 7/507 (1.38%) | 4/505 (0.79%) |
| Hyperparathyroidism secondary | 9/507 (1.78%) | 8/505 (1.58%) |
| Eye disorders | | |
| Cataract | 12/507 (2.37%) | 6/505 (1.19%) |
| Eye haemorrhage | 7/507 (1.38%) | 0/505 (0%) |
| Gastrointestinal disorders | | |
| Abdominal discomfort | 9/507 (1.78%) | 0/505 (0%) |
| Abdominal distension | 16/507 (3.16%) | 16/505 (3.17%) |
| Abdominal pain | 18/507 (3.55%) | 19/505 (3.76%) |
| Abdominal pain upper | 14/507 (2.76%) | 13/505 (2.57%) |
| Constipation | 55/507 (10.85%) | 38/505 (7.52%) |
| Diarrhoea | 42/507 (8.28%) | 41/505 (8.12%) |
| Dyspepsia | 16/507 (3.16%) | 21/505 (4.16%) |
| Faeces discoloured | 4/507 (0.79%) | 11/505 (2.18%) |
| Flatulence | 12/507 (2.37%) | 15/505 (2.97%) |
| Gastritis | 20/507 (3.94%) | 22/505 (4.36%) |
| Gastrooesophageal reflux disease | 11/507 (2.17%) | 2/505 (0.4%) |

| | AST-120 | Placebo |
|---|---|---|
| | Affected/At Risk (%) | Affected/At Risk (%) |
| Nausea | 45/507 (8.88%) | 45/505 (8.91%) |
| Vomiting | 28/507 (5.52%) | 36/505 (7.13%) |
| General disorders | | |
| Asthenia | 14/507 (2.76%) | 20/505 (3.96%) |
| Chest pain | 7/507 (1.38%) | 6/505 (1.19%) |
| Chills | 6/507 (1.18%) | 1/505 (0.2%) |
| Fatigue | 22/507 (4.34%) | 14/505 (2.77%) |
| Oedema | 13/507 (2.56%) | 13/505 (2.57%) |
| Oedema peripheral | 46/507 (9.07%) | 57/505 (11.29%) |
| Pyrexia | 8/507 (1.58%) | 9/505 (1.78%) |
| Infections and infestations | | |
| Bronchitis | 14/507 (2.76%) | 19/505 (3.76%) |
| Cellulitis | 7/507 (1.38%) | 5/505 (0.99%) |
| Cystitis | 6/507 (1.18%) | 4/505 (0.79%) |
| Gastroenteritis | 9/507 (1.78%) | 6/505 (1.19%) |
| Herpes zoster | 7/507 (1.38%) | 3/505 (0.59%) |
| Influenza | 26/507 (5.13%) | 21/505 (4.16%) |
| Nasopharyngitis | 21/507 (4.14%) | 14/505 (2.77%) |
| Pharyngitis | 11/507 (2.17%) | 8/505 (1.58%) |
| Pneumonia | 5/507 (0.99%) | 6/505 (1.19%) |
| Respiratory tract infection | 9/507 (1.78%) | 9/505 (1.78%) |
| Respiratory tract infection viral | 4/507 (0.79%) | 6/505 (1.19%) |
| Sinusitis | 14/507 (2.76%) | 5/505 (0.99%) |
| Upper respiratory tract infection | 25/507 (4.93%) | 19/505 (3.76%) |
| Urinary tract infection | 28/507 (5.52%) | 33/505 (6.53%) |
| Injury, poisoning and procedural complications | | |

| | AST-120 | Placebo |
|---|---|---|
| | Affected/At Risk (%) | Affected/At Risk (%) |
| Contusion | 8/507 (1.58%) | 2/505 (0.4%) |
| Fall | 6/507 (1.18%) | 5/505 (0.99%) |
| Investigations | | |
| Blood bicarbonate decreased | 7/507 (1.38%) | 3/505 (0.59%) |
| Blood creatine phosphokinase increased | 12/507 (2.37%) | 9/505 (1.78%) |
| Blood pressure increased | 10/507 (1.97%) | 9/505 (1.78%) |
| Weight increased | 6/507 (1.18%) | 3/505 (0.59%) |
| Metabolism and nutrition disorders | | |
| Acidosis | 4/507 (0.79%) | 7/505 (1.39%) |
| Decreased appetite | 15/507 (2.96%) | 16/505 (3.17%) |
| Diabetes mellitus | 6/507 (1.18%) | 4/505 (0.79%) |
| Dyslipidaemia | 6/507 (1.18%) | 7/505 (1.39%) |
| Gout | 24/507 (4.73%) | 19/505 (3.76%) |
| Hypercalcaemia | 7/507 (1.38%) | 5/505 (0.99%) |
| Hypercholesterolaemia | 13/507 (2.56%) | 6/505 (1.19%) |
| Hyperglycaemia | 15/507 (2.96%) | 14/505 (2.77%) |
| Hyperkalaemia | 43/507 (8.48%) | 35/505 (6.93%) |
| Hyperphosphataemia | 22/507 (4.34%) | 17/505 (3.37%) |
| Hypertriglyceridaemia | 6/507 (1.18%) | 8/505 (1.58%) |
| Hypocalcaemia | 7/507 (1.38%) | 8/505 (1.58%) |
| Hypoglycaemia | 12/507 (2.37%) | 19/505 (3.76%) |
| Hypokalaemia | 7/507 (1.38%) | 6/505 (1.19%) |
| Metabolic acidosis | 17/507 (3.35%) | 14/505 (2.77%) |
| Vitamin D deficiency | 15/507 (2.96%) | 24/505 (4.75%) |
| Musculoskeletal and connective tissue disorders | | |
| Arthralgia | 19/507 (3.75%) | 21/505 (4.16%) |

| | AST-120 | Placebo |
|---|---|---|
| | Affected/At Risk (%) | Affected/At Risk (%) |
| Back pain | 17/507 (3.35%) | 18/505 (3.56%) |
| Muscle spasms | 28/507 (5.52%) | 27/505 (5.35%) |
| Musculoskeletal pain | 6/507 (1.18%) | 8/505 (1.58%) |
| Myalgia | 5/507 (0.99%) | 6/505 (1.19%) |
| Osteoarthritis | 7/507 (1.38%) | 5/505 (0.99%) |
| Pain in extremity | 17/507 (3.35%) | 16/505 (3.17%) |
| Nervous system disorders | | |
| Dizziness | 16/507 (3.16%) | 15/505 (2.97%) |
| Headache | 17/507 (3.35%) | 21/505 (4.16%) |
| Hypoaesthesia | 7/507 (1.38%) | 0/505 (0%) |
| Psychiatric disorders | | |
| Anxiety | 9/507 (1.78%) | 5/505 (0.99%) |
| Depression | 9/507 (1.78%) | 12/505 (2.38%) |
| Insomnia | 14/507 (2.76%) | 13/505 (2.57%) |
| Renal and urinary disorders | | |
| Haematuria | 1/507 (0.2%) | 6/505 (1.19%) |
| Proteinuria | 6/507 (1.18%) | 1/505 (0.2%) |
| Renal failure acute | 1/507 (0.2%) | 6/505 (1.19%) |
| Renal failure chronic | 40/507 (7.89%) | 40/505 (7.92%) |
| Respiratory, thoracic and mediastinal disorders | | |
| Cough | 31/507 (6.11%) | 21/505 (4.16%) |
| Dyspnoea | 18/507 (3.55%) | 21/505 (4.16%) |
| Skin and subcutaneous tissue disorders | | |
| Dermatitis | 8/507 (1.58%) | 2/505 (0.4%) |
| Pruritus | 22/507 (4.34%) | 18/505 (3.56%) |
| Rash | 9/507 (1.78%) | 12/505 (2.38%) |

| | AST-120 | Placebo |
|---|---|---|
| | Affected/At Risk (%) | Affected/At Risk (%) |
| Surgical and medical procedures | | |
| Arteriovenous fistula operation | 16/507 (3.16%) | 22/505 (4.36%) |
| Vascular disorders | | |
| Hypertension | 54/507 (10.65%) | 49/505 (9.7%) |
| Hypertensive crisis | 7/507 (1.38%) | 2/505 (0.4%) |
| Hypotension | 15/507 (2.96%) | 12/505 (2.38%) |

## Limitations and Caveats

[Not specified]

## More Information

Certain Agreements:

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

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

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