| | | Xanomeline Low | Xanomeline High |
|--|---------|----------------|-----------------|
| | Placebo | Dose | Dose |
| | n | n | n |
| Participants in population | 86 | 84 | 84 |
| Cardiac Disorders | 12 | 12 | 10 |
| | 13 | 13 | 18 |
| Atrial Fibrillation | 1 | 1 | 3 |
| Atrial Flutter | 0 | 1 | 1 |
| Atrial Hypertrophy | 1 | 0 | 0 |
| Atrioventricular Block First Degree | 1 | 1 | 0 |
| Atrioventricular Block Second Degree | 2 | 0 | 3 |
| Bradycardia | 1 | 0 | 0 |
| Bundle Branch Block Left | 1 | 0 | 0 |
| Bundle Branch Block Right | 1 | 1 | 0 |
| Cardiac Disorder | 0 | 0 | 1 |
| Cardiac Failure Congestive | 1 | 0 | 0 |
| Myocardial Infarction | 4 | 2 | 4 |
| Palpitations | 0 | 2 | 0 |
| Sinus Arrhythmia | 1 | 0 | 0 |
| Sinus Bradycardia | 2 | 7 | 8 |
| Supraventricular Extrasystoles | 1 | 1 | 1 |
| Supraventricular Tachycardia | 0 | 1 | 0 |
| Tachycardia | 1 | 0 | 0 |
| Ventricular Extrasystoles | 0 | 2 | 1 |
| Ventricular Hypertrophy | 1 | 0 | 0 |
| Wolff-Parkinson-White Syndrome | 0 | 1 | 0 |
| Congenital, Familial and Genetic Disorders | 0 | 1 | 2 |
| Ventricular Septal Defect | 0 | 1 | 2 |
| Ear and Labyrinth Disorders | 1 | 2 | 1 |
| Cerumen Impaction | 0 | 1 | 0 |
| Ear Pain | 1 | 0 | 0 |
| Tinnitus | 0 | 1 | 0 |
| Vertigo | 0 | 1 | 1 |
| Eye Disorders | 4 | 2 | 1 |
| Conjunctival Haemorrhage | 0 | 1 | 0 |
| Conjunctivitis | 2 | 0 | 0 |

| | Xanomeline Low | Xanomeline High | |
|--|----------------|-----------------|------|
| | Placebo | Dose | Dose |
| | n | n | n |
| Eye Disorders | 4 | 2 | 1 |
| Eye Allergy | 1 | 0 | 0 |
| Eye Pruritus | 1 | 0 | 0 |
| Eye Swelling | 1 | 0 | 0 |
| Glaucoma | 1 | 0 | 0 |
| Vision Blurred | 0 | 1 | 1 |
| Gastrointestinal Disorders | 17 | 15 | 21 |
| Abdominal Discomfort | 0 | 0 | 1 |
| Abdominal Pain | 1 | 3 | 1 |
| Constipation | 1 | 0 | 0 |
| Diarrhoea | 9 | 5 | 4 |
| Dyspepsia | 1 | 1 | 1 |
| Dysphagia | 0 | 1 | 0 |
| Flatulence | 1 | 0 | 0 |
| Gastrointestinal Haemorrhage | 0 | 0 | 1 |
| Gastrooesophageal Reflux Disease | 1 | 0 | 0 |
| Glossitis | 1 | 0 | 0 |
| Hiatus Hernia | 1 | 0 | 0 |
| Nausea | 3 | 3 | 6 |
| Rectal Haemorrhage | 0 | 1 | 0 |
| Salivary Hypersecretion | 0 | 0 | 4 |
| Stomach Discomfort | 0 | 0 | 1 |
| Vomiting | 3 | 3 | 7 |
| General Disorders and Administration Site Conditions | 21 | 47 | 40 |
| Application Site Bleeding | 0 | 1 | 0 |
| Application Site Dermatitis | 5 | 9 | 7 |
| Application Site Desquamation | 0 | 1 | 0 |
| Application Site Discharge | 0 | 0 | 1 |
| Application Site Discolouration | 0 | 1 | 0 |
| Application Site Erythema | 3 | 12 | 15 |
| Application Site Induration | 1 | 0 | 0 |
| Application Site Irritation | 3 | 9 | 9 |
| Application Site Pain | 0 | 0 | 2 |
| Application Site Perspiration | 0 | 0 | 2 |
| Application Site Pruritus | 6 | 22 | 22 |

| | Placebo | Xanomeline Low Dose | Xanomeline High Dose |
|--|---------|------------------------|-------------------------|
| | n | n | n |
| General Disorders and Administration Site Conditions | 21 | 47 | 40 |
| Application Site Reaction | 1 | 0 | 1 |
| Application Site Keaction Application Site Swelling | 0 | 1 | 2 |
| • • | Ť | _ | |
| Application Site Urticaria | 0 1 | 2 4 | 1 |
| Application Site Vesicles | 1 | • | 6 |
| Application Site Warmth | 0 | 1 | 0 |
| Asthenia | I | 0 | 1 |
| Chest Discomfort | 0 | 0 | 2 |
| Chest Pain | 0 | 0 | 2 |
| Chills | 1 | 1 | 1 |
| Cyst | 0 | 1 | 0 |
| Fatigue | 1 | 5 | 5 |
| Feeling Abnormal | 0 | 0 | 1 |
| Feeling Cold | 0 | 0 | 1 |
| Inflammation | 0 | 1 | 0 |
| Malaise | 0 | 1 | 2 |
| Oedema | 0 | 2 | 0 |
| Oedema Peripheral | 2 | 1 | 2 |
| Pain | 0 | 1 | 1 |
| Pyrexia | 2 | 0 | 1 |
| Secretion Discharge | 0 | 1 | 0 |
| Sudden Death | 0 | 1 | 0 |
| Swelling | 0 | 1 | 0 |
| Ulcer | 0 | 1 | 0 |
| Hepatobiliary Disorders | 1 | 0 | 0 |
| Hyperbilirubinaemia | 1 | 0 | 0 |
| Immune System Disorders | 0 | 1 | 1 |
| Hypersensitivity | 0 | 1 | 0 |
| Seasonal Allergy | 0 | 0 | 1 |
| Infections and Infestations | 16 | 10 | 13 |
| Bronchitis | 1 | 0 | 0 |
| Cellulitis | 0 | 1 | 0 |
| Cervicitis | 1 | 0 | 0 |
| Cystitis | 1 | 0 | 1 |
| Ear Infection | 2 | 0 | 0 |

| | | Xanomeline Low | Xanomeline High |
|--|---------|----------------|-----------------|
| | Placebo | Dose | Dose |
| | n | n | n |
| Infections and Infestations | 16 | 10 | 13 |
| Gastroenteritis Viral | 1 | 0 | 0 |
| Hordeolum | 0 | 0 | 1 |
| Influenza | 1 | 1 | 1 |
| Localised Infection | 1 | 1 | 0 |
| Lower Respiratory Tract Infection | 0 | 0 | 1 |
| Nasopharyngitis | 2 | 4 | 6 |
| Onychomycosis | 0 | 1 | 0 |
| Pneumonia | 0 | 1 | 0 |
| Rhinitis | 0 | 0 | 1 |
| Upper Respiratory Tract Infection | 6 | 1 | 3 |
| Urinary Tract Infection | 2 | 0 | 1 |
| Vaginal Mycosis | 1 | 0 | 0 |
| Viral Infection | 0 | 1 | 0 |
| Injury, Poisoning and Procedural Complications | 4 | 5 | 5 |
| Contusion | 1 | 1 | 2 |
| Excoriation | 2 | 1 | 1 |
| Facial Bones Fracture | 0 | 0 | 1 |
| Fall | 1 | 2 | 1 |
| Hip Fracture | 1 | 0 | 2 |
| Joint Dislocation | 0 | 1 | 0 |
| Skin Laceration | 1 | 2 | 0 |
| Wound | 0 | 1 | 0 |
| Investigations | 10 | 7 | 6 |
| Biopsy | 0 | 0 | 1 |
| Biopsy Prostate | 0 | 0 | 1 |
| Blood Alkaline Phosphatase Increased | 1 | 0 | 0 |
| Blood Cholesterol Increased | 0 | 0 | 1 |
| Blood Creatine Phosphokinase Increased | 1 | 0 | 0 |
| Blood Glucose Increased | 0 | 1 | 1 |
| Blood Urine Present | 1 | 0 | 0 |
| Body Temperature Increased | 0 | 1 | 0 |
| Cystoscopy | 1 | 0 | 0 |
| Electrocardiogram St Segment Depression | 4 | 1 | 0 |
| Electrocardiogram t Wave Amplitude Decreased | 1 | 1 | 0 |

| | DI I | Xanomeline Low | Xanomeline High |
|---|---------|----------------|-----------------|
| | Placebo | Dose | Dose |
| I | 10 | n 7 | n |
| Investigations Electrocardiogram t Wave Inversion | 2 | 1 | 6 |
| Heart Rate Increased | 1 | 0 | 0 |
| Heart Rate Irregular | 1 | 0 | 0 |
| · · | 0 | 1 | 0 |
| Nasal Mucosa Biopsy | 0 | 1 | 0 |
| Neutrophil Count Increased | | 1 | Ů |
| Urine Analysis Abnormal | 0 | 1 | 0 |
| Weight Decreased | 0 | 0 | 1 |
| White Blood Cell Count Increased | 0 | 1 | 0 |
| Metabolism and Nutrition Disorders | 6 | 1 | 3 |
| Decreased Appetite | 1 | 0 | 1 |
| Dehydration | 1 | 0 | 0 |
| Diabetes Mellitus | 1 | 0 | 0 |
| Food Craving | 1 | 1 | 0 |
| Hypercholesterolaemia | 0 | 0 | 1 |
| Hyponatraemia | 1 | 0 | 0 |
| Increased Appetite | 1 | 0 | 1 |
| Musculoskeletal and Connective Tissue Disorders | 5 | 7 | 8 |
| Arthralgia | 1 | 2 | 1 |
| Arthritis | 1 | 0 | 1 |
| Back Pain | 1 | 1 | 3 |
| Flank Pain | 0 | 0 | 2 |
| Muscle Spasms | 0 | 1 | 1 |
| Muscular Weakness | 0 | 1 | 0 |
| Myalgia | 0 | 0 | 1 |
| Pain in Extremity | 1 | 0 | 0 |
| Shoulder Pain | 1 | 2 | 0 |
| Neoplasms Benign, Malignant and Unspecified (Incl | 0 | 2 | 1 |
| Cysts and Polyps) | | | |
| Colon Cancer | 0 | 1 | 0 |
| Malignant Fibrous Histiocytoma | 0 | 1 | 0 |
| Prostate Cancer | 0 | 0 | 1 |
| Nervous System Disorders | 12 | 20 | 27 |
| Amnesia | 0 | 0 | 1 |
| Balance Disorder | 0 | 1 | 0 |
| Burning Sensation | 0 | 0 | 2 |

| | | Xanomeline Low | Xanomeline High |
|--|---------|----------------|-----------------|
| | Placebo | Dose | Dose |
| | n | n | n |
| Nervous System Disorders | 12 | 20 | 27 |
| Cognitive Disorder | 0 | 0 | 1 |
| Complex Partial Seizures | 0 | 1 | 0 |
| Coordination Abnormal | 0 | 1 | 0 |
| Dizziness | 2 | 8 | 12 |
| Headache | 7 | 3 | 6 |
| Hemianopia Homonymous | 0 | 1 | 0 |
| Hypersomnia | 0 | 0 | 1 |
| Lethargy | 0 | 1 | 1 |
| Paraesthesia | 0 | 0 | 1 |
| Paraesthesia Oral | 0 | 1 | 0 |
| Parkinson's Disease | 1 | 0 | 0 |
| Parosmia | 0 | 0 | 1 |
| Partial Seizures with Secondary Generalisation | 0 | 0 | 1 |
| Psychomotor Hyperactivity | 1 | 0 | 0 |
| Somnolence | 2 | 3 | 1 |
| Stupor | 0 | 1 | 0 |
| Syncope | 0 | 4 | 3 |
| Syncope Vasovagal | 0 | 0 | 1 |
| Transient Ischaemic Attack | 0 | 2 | 1 |
| Psychiatric Disorders | 10 | 10 | 9 |
| Agitation | 2 | 2 | 1 |
| Anxiety | 1 | 3 | 0 |
| Completed Suicide | 1 | 0 | 0 |
| Confusional State | 2 | 3 | 1 |
| Delirium | 0 | 0 | 1 |
| Delusion | 1 | 0 | 1 |
| Depressed Mood | 0 | 1 | 1 |
| Disorientation | 1 | 0 | 0 |
| Hallucination | 0 | 0 | 1 |
| Hallucination, Visual | 0 | 0 | 1 |
| Insomnia | 2 | 0 | 2 |
| Irritability | 1 | 1 | 0 |
| Libido Decreased | 0 | 0 | 1 |
| Listless | 0 | 0 | 1 |

| | DI I | Xanomeline Low Dose | Xanomeline High Dose |
|---|---------|------------------------|-------------------------|
| | Placebo | | |
| | n | n | n |
| Psychiatric Disorders | 10 | 10 | 9 |
| Nightmare | 0 | 0 | 1 |
| Restlessness | 0 | 1 | 0 |
| Renal and Urinary Disorders | 4 | 4 | 3 |
| Calculus Urethral | 0 | 0 | 1 |
| Dysuria | 1 | 1 | 0 |
| Enuresis | 0 | 1 | 0 |
| Incontinence | 0 | 1 | 0 |
| Micturition Urgency | 1 | 1 | 1 |
| Nephrolithiasis | 1 | 0 | 1 |
| Pollakiuria | 1 | 0 | 0 |
| Reproductive System and Breast Disorders | 2 | 0 | 1 |
| Benign Prostatic Hyperplasia | 1 | 0 | 1 |
| Pelvic Pain | 1 | 0 | 0 |
| Respiratory, Thoracic and Mediastinal Disorders | 10 | 10 | 10 |
| Allergic Granulomatous Angiitis | 0 | 0 | 1 |
| Cough | 3 | 6 | 5 |
| Dysphonia | 0 | 1 | 0 |
| Dyspnoea | 1 | 1 | 1 |
| Emphysema | 1 | 0 | 0 |
| Epistaxis | 0 | 1 | 2 |
| Haemoptysis | 1 | 0 | 0 |
| Nasal Congestion | 3 | 1 | 3 |
| Pharyngeal Erythema | 0 | 0 | 1 |
| Pharyngolaryngeal Pain | 0 | 1 | 1 |
| Postnasal Drip | 1 | 0 | 0 |
| Productive Cough | 0 | 0 | 1 |
| Rales | 1 | 0 | 0 |
| Respiratory Tract Congestion | 0 | 0 | 1 |
| Rhinorrhoea | 0 | 1 | 1 |
| Skin and Subcutaneous Tissue Disorders | 21 | 42 | 42 |
| Actinic Keratosis | 0 | 0 | 1 |
| Alopecia | 1 | 0 | 0 |
| Blister | 0 | 5 | 1 |
| Cold Sweat | 1 | 0 | 0 |

| | | Xanomeline Low | Xanomeline High |
|--|---------|----------------|-----------------|
| | Placebo | Dose | Dose |
| | n | n | n |
| Skin and Subcutaneous Tissue Disorders | 21 | 42 | 42 |
| Dermatitis Atopic | 1 | 0 | 0 |
| Dermatitis Contact | 0 | 1 | 0 |
| Drug Eruption | 1 | 0 | 0 |
| Erythema | 9 | 15 | 14 |
| Hyperhidrosis | 2 | 4 | 8 |
| Pruritus | 8 | 23 | 26 |
| Pruritus Generalised | 0 | 1 | 1 |
| Rash | 5 | 13 | 11 |
| Rash Erythematous | 0 | 2 | 0 |
| Rash Maculo-Papular | 0 | 0 | 1 |
| Rash Papular | 0 | 0 | 1 |
| Rash Pruritic | 0 | 1 | 2 |
| Skin Exfoliation | 0 | 1 | 0 |
| Skin Irritation | 3 | 6 | 5 |
| Skin Odour Abnormal | 0 | 0 | 1 |
| Skin Ulcer | 1 | 0 | 0 |
| Urticaria | 0 | 1 | 1 |
| Social Circumstances | 0 | 0 | 1 |
| Alcohol Use | 0 | 0 | 1 |
| Surgical and Medical Procedures | 2 | 1 | 2 |
| Acrochordon Excision | 0 | 0 | 1 |
| Cataract Operation | 1 | 1 | 0 |
| Eye Laser Surgery | 1 | 0 | 0 |
| Skin Lesion Excision | 0 | 0 | 1 |
| Vascular Disorders | 3 | 3 | 2 |
| Hot Flush | 0 | 1 | 0 |
| Hypertension | 1 | 1 | 1 |
| Hypotension | 2 | 1 | 0 |
| Orthostatic Hypotension | 1 | 0 | 0 |
| Wound Haemorrhage | 0 | 0 | 1 |
| Every subject is counted a single time for each applicable row and column. | | | |