

Table 14-5.01
Incidence of Treatment Emergent Adverse Events by Treatment Group

System Organ Class/ Preferred Term	Placebo (N=86)		Xanomeline Low (N=84)		Xanomeline High (N=84)		Fisher's Exact p-values Placebo vs. Placebo vs. Low Dose High Dose	
	n(%)	[AEs]	n(%)	[AEs]	n(%)	[AEs]		
ANY BODY SYSTEM	65 (75.6%)	[281]	77 (91.7%)	[412]	76 (90.5%)	[433]	0.007*	0.014*
CARDIAC DISORDERS	12 (14.0%)	[26]	13 (15.5%)	[30]	15 (17.9%)	[30]	0.831	0.534
SINUS BRADYCARDIA	2 (2.3%)	[2]	7 (8.3%)	[10]	8 (9.5%)	[12]	0.097*	0.056*
MYOCARDIAL INFARCTION	4 (4.7%)	[4]	2 (2.4%)	[4]	4 (4.8%)	[8]	0.682	>0.99
ATRIAL FIBRILLATION	1 (1.2%)	[1]	1 (1.2%)	[1]	3 (3.6%)	[5]	>0.99	0.365
ATRIAL FLUTTER	0		1 (1.2%)	[1]	1 (1.2%)	[2]	0.494	0.494
CARDIAC DISORDER	0		0		1 (1.2%)	[1]		0.494
SUPRAVENTRICULAR	1 (1.2%)	[2]	1 (1.2%)	[2]	1 (1.2%)	[1]	>0.99	>0.99
EXTRASYSTOLES								
VENTRICULAR EXTRASYSTOLES	0		2 (2.4%)	[4]	1 (1.2%)	[1]	0.243	0.494
ATRIAL HYPERTROPHY	1 (1.2%)	[2]	0		0		>0.99	>0.99
ATRIOVENTRICULAR BLOCK	1 (1.2%)	[1]	1 (1.2%)	[1]	0		>0.99	>0.99
FIRST DEGREE								
ATRIOVENTRICULAR BLOCK	1 (1.2%)	[1]	0		0		>0.99	>0.99
SECOND DEGREE								
BRADYCARDIA	1 (1.2%)	[4]	0		0		>0.99	>0.99
BUNDLE BRANCH BLOCK LEFT	1 (1.2%)	[1]	0		0		>0.99	>0.99
BUNDLE BRANCH BLOCK RIGHT	1 (1.2%)	[2]	1 (1.2%)	[1]	0		>0.99	>0.99

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	n(%)	[AEs]	n(%)	[AEs]	n(%)	[AEs]		
CARDIAC FAILURE	1 (1.2%)	[1]	0		0		>0.99	>0.99
CONGESTIVE								
PALPITATIONS	0		2 (2.4%)	[2]	0		0.243	
SINUS ARRHYTHMIA	1 (1.2%)	[2]	0		0		>0.99	>0.99
SUPRAVENTRICULAR	0		1 (1.2%)	[2]	0		0.494	
TACHYCARDIA								
TACHYCARDIA	1 (1.2%)	[2]	0		0		>0.99	>0.99
VENTRICULAR HYPERTROPHY	1 (1.2%)	[1]	0		0		>0.99	>0.99
WOLFF-PARKINSON-WHITE	0		1 (1.2%)	[2]	0		0.494	
SYNDROME								
CONGENITAL, FAMILIAL AND	0		1 (1.2%)	[1]	2 (2.4%)	[2]	0.494	0.243
GENETIC DISORDE								
VENTRICULAR SEPTAL DEFECT	0		1 (1.2%)	[1]	2 (2.4%)	[2]	0.494	0.243
EAR AND LABYRINTH DISORDERS	1 (1.2%)	[2]	2 (2.4%)	[2]	1 (1.2%)	[1]	0.618	>0.99
VERTIGO	0		1 (1.2%)	[1]	1 (1.2%)	[1]	0.494	0.494
CERUMEN IMPACTION	0		1 (1.2%)	[1]	0		0.494	
EAR PAIN	1 (1.2%)	[2]	0		0		>0.99	>0.99
EYE DISORDERS	2 (2.3%)	[5]	2 (2.4%)	[2]	1 (1.2%)	[2]	>0.99	>0.99

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	n(%)	[AEs]	n(%)	[AEs]	n(%)	[AEs]	Low Dose	High Dose
VISION BLURRED	0		1 (1.2%)	[1]	1 (1.2%)	[2]	0.494	0.494
CONJUNCTIVAL HAEMORRHAGE	0		1 (1.2%)	[1]	0		0.494	
CONJUNCTIVITIS	1 (1.2%)	[2]	0		0		>0.99	>0.99
EYE ALLERGY	1 (1.2%)	[1]	0		0		>0.99	>0.99
EYE PRURITUS	1 (1.2%)	[1]	0		0		>0.99	>0.99
EYE SWELLING	1 (1.2%)	[1]	0		0		>0.99	>0.99
GASTROINTESTINAL DISORDERS	17 (19.8%)	[26]	14 (16.7%)	[22]	20 (23.8%)	[36]	0.692	0.58
VOMITING	3 (3.5%)	[3]	3 (3.6%)	[4]	7 (8.3%)	[9]	>0.99	0.209
NAUSEA	3 (3.5%)	[3]	3 (3.6%)	[5]	6 (7.1%)	[13]	>0.99	0.326
DIARRHOEA	9 (10.5%)	[10]	4 (4.8%)	[5]	4 (4.8%)	[4]	0.248	0.248
SALIVARY HYPERSECRETION	0		0		4 (4.8%)	[5]		0.058*
ABDOMINAL DISCOMFORT	0		0		1 (1.2%)	[1]		0.494
ABDOMINAL PAIN	1 (1.2%)	[1]	3 (3.6%)	[3]	1 (1.2%)	[2]	0.365	>0.99
GASTROINTESTINAL HAEMORRHAGE	0		0		1 (1.2%)	[1]		0.494
STOMACH DISCOMFORT	0		0		1 (1.2%)	[1]		0.494
CONSTIPATION	1 (1.2%)	[1]	0		0		>0.99	>0.99
DYSPEPSIA	1 (1.2%)	[2]	1 (1.2%)	[2]	0		>0.99	>0.99
DYSPHAGIA	0		1 (1.2%)	[1]	0		0.494	
FLATULENCE	1 (1.2%)	[2]	0		0		>0.99	>0.99

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	n(%)	[AEs]	n(%)	[AEs]	n(%)	[AEs]		
GASTROESOPHAGEAL REFLUX DISEASE	1 (1.2%)	[1]	0		0		>0.99	>0.99
GLOSSITIS	1 (1.2%)	[1]	0		0		>0.99	>0.99
HIATUS HERNIA	1 (1.2%)	[2]	0		0		>0.99	>0.99
RECTAL HAEMORRHAGE	0		1 (1.2%)	[2]	0		0.494	
GENERAL DISORDERS AND ADMINISTRATION SIT	21 (24.4%)	[46]	47 (56.0%)	[118]	40 (47.6%)	[124]	0.000*	0.002*
APPLICATION SITE PRURITUS	6 (7.0%)	[10]	22 (26.2%)	[32]	22 (26.2%)	[35]	0.001*	0.001*
APPLICATION SITE ERYTHEMA	3 (3.5%)	[3]	12 (14.3%)	[20]	15 (17.9%)	[23]	0.015*	0.003*
APPLICATION SITE IRRITATION	3 (3.5%)	[7]	9 (10.7%)	[18]	9 (10.7%)	[16]	0.078*	0.078*
APPLICATION SITE DERMATITIS	5 (5.8%)	[9]	9 (10.7%)	[15]	7 (8.3%)	[12]	0.277	0.563
APPLICATION SITE VESICLES	1 (1.2%)	[2]	4 (4.8%)	[5]	6 (7.1%)	[6]	0.208	0.062*
FATIGUE	1 (1.2%)	[2]	5 (6.0%)	[5]	5 (6.0%)	[5]	0.115*	0.115*
APPLICATION SITE PAIN	0		0		2 (2.4%)	[2]		0.243
APPLICATION SITE PERSPIRATION	0		0		2 (2.4%)	[3]		0.243
APPLICATION SITE SWELLING	0		1 (1.2%)	[1]	2 (2.4%)	[3]	0.494	0.243
CHEST DISCOMFORT	0		0		2 (2.4%)	[2]		0.243

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	n(%)	[AEs]	n(%)	[AEs]	n(%)	[AEs]		
CHEST PAIN	0		0		2 (2.4%)	[2]		0.243
MALAISE	0		1 (1.2%)	[2]	2 (2.4%)	[3]	0.494	0.243
OEDEMA PERIPHERAL	2 (2.3%)	[3]	1 (1.2%)	[1]	2 (2.4%)	[3]	>0.99	>0.99
APPLICATION SITE	0		0		1 (1.2%)	[1]		0.494
DISCHARGE								
APPLICATION SITE REACTION	1 (1.2%)	[2]	0		1 (1.2%)	[1]	>0.99	>0.99
APPLICATION SITE	0		2 (2.4%)	[2]	1 (1.2%)	[1]	0.243	0.494
URTICARIA								
ASTHENIA	1 (1.2%)	[2]	0		1 (1.2%)	[1]	>0.99	>0.99
CHILLS	1 (1.2%)	[3]	1 (1.2%)	[2]	1 (1.2%)	[1]	>0.99	>0.99
FEELING ABNORMAL	0		0		1 (1.2%)	[1]		0.494
FEELING COLD	0		0		1 (1.2%)	[1]		0.494
PAIN	0		1 (1.2%)	[2]	1 (1.2%)	[1]	0.494	0.494
PYREXIA	2 (2.3%)	[2]	0		1 (1.2%)	[1]	0.497	>0.99
APPLICATION SITE BLEEDING	0		1 (1.2%)	[1]	0		0.494	
APPLICATION SITE	0		1 (1.2%)	[1]	0		0.494	
DESQUAMATION								
APPLICATION SITE	0		1 (1.2%)	[1]	0		0.494	
DISCOLOURATION								
APPLICATION SITE	1 (1.2%)	[1]	0		0		>0.99	>0.99
INDURATION								

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	n(%)	[AEs]	n(%)	[AEs]	n(%)	[AEs]		
APPLICATION SITE WARMTH	0		1 (1.2%)	[2]	0		0.494	
INFLAMMATION	0		1 (1.2%)	[1]	0		0.494	
OEDEMA	0		2 (2.4%)	[2]	0		0.243	
SECRETION DISCHARGE	0		1 (1.2%)	[2]	0		0.494	
SUDDEN DEATH	0		1 (1.2%)	[1]	0		0.494	
SWELLING	0		1 (1.2%)	[1]	0		0.494	
ULCER	0		1 (1.2%)	[1]	0		0.494	
HEPATOBIILIARY DISORDERS	1 (1.2%)	[1]	0		0		>0.99	>0.99
HYPERBILIRUBINAEMIA	1 (1.2%)	[1]	0		0		>0.99	>0.99
IMMUNE SYSTEM DISORDERS	0		1 (1.2%)	[2]	0		0.494	
HYPERSENSITIVITY	0		1 (1.2%)	[2]	0		0.494	
INFECTIONS AND INFESTATIONS	16 (18.6%)	[35]	9 (10.7%)	[16]	13 (15.5%)	[20]	0.194	0.685
NASOPHARYNGITIS	2 (2.3%)	[4]	4 (4.8%)	[9]	6 (7.1%)	[8]	0.441	0.166
UPPER RESPIRATORY TRACT INFECTION	6 (7.0%)	[12]	1 (1.2%)	[2]	3 (3.6%)	[5]	0.117*	0.496
CYSTITIS	1 (1.2%)	[1]	0		1 (1.2%)	[1]	>0.99	>0.99
HORDEOLUM	0		0		1 (1.2%)	[1]		0.494
INFLUENZA	1 (1.2%)	[2]	1 (1.2%)	[1]	1 (1.2%)	[1]	>0.99	>0.99

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	n(%)	[AEs]	n(%)	[AEs]	n(%)	[AEs]		
LOWER RESPIRATORY TRACT INFECTION	0		0		1 (1.2%)	[2]		0.494
RHINITIS	0		0		1 (1.2%)	[1]		0.494
URINARY TRACT INFECTION	2 (2.3%)	[4]	0		1 (1.2%)	[1]	0.497	>0.99
BRONCHITIS	1 (1.2%)	[1]	0		0		>0.99	>0.99
CELLULITIS	0		1 (1.2%)	[1]	0		0.494	
CERVICITIS	1 (1.2%)	[2]	0		0		>0.99	>0.99
EAR INFECTION	2 (2.3%)	[4]	0		0		0.497	0.497
GASTROENTERITIS VIRAL	1 (1.2%)	[1]	0		0		>0.99	>0.99
LOCALISED INFECTION	1 (1.2%)	[2]	0		0		>0.99	>0.99
PNEUMONIA	0		1 (1.2%)	[2]	0		0.494	
VAGINAL MYCOSIS	1 (1.2%)	[2]	0		0		>0.99	>0.99
VIRAL INFECTION	0		1 (1.2%)	[1]	0		0.494	
INJURY, POISONING AND PROCEDURAL COMPLIC	4 (4.7%)	[9]	5 (6.0%)	[12]	5 (6.0%)	[8]	0.745	0.745
CONTUSION	1 (1.2%)	[1]	1 (1.2%)	[3]	2 (2.4%)	[3]	>0.99	0.618
HIP FRACTURE	1 (1.2%)	[2]	0		2 (2.4%)	[2]	>0.99	0.618
EXCORIATION	2 (2.3%)	[3]	1 (1.2%)	[2]	1 (1.2%)	[1]	>0.99	>0.99
FACIAL BONES FRACTURE	0		0		1 (1.2%)	[1]		0.494
FALL	1 (1.2%)	[2]	2 (2.4%)	[2]	1 (1.2%)	[1]	0.618	>0.99

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	n(%)	[AEs]	n(%)	[AEs]	n(%)	[AEs]		
JOINT DISLOCATION	0		1 (1.2%)	[1]	0		0.494	
SKIN LACERATION	1 (1.2%)	[1]	2 (2.4%)	[2]	0		0.618	>0.99
WOUND	0		1 (1.2%)	[2]	0		0.494	
INVESTIGATIONS	10 (11.6%)	[19]	6 (7.1%)	[7]	6 (7.1%)	[8]	0.432	0.432
BIOPSY	0		0		1 (1.2%)	[1]		0.494
BIOPSY PROSTATE	0		0		1 (1.2%)	[1]		0.494
BLOOD CHOLESTEROL	0		0		1 (1.2%)	[1]		0.494
INCREASED								
BLOOD GLUCOSE INCREASED	0		1 (1.2%)	[1]	1 (1.2%)	[2]	0.494	0.494
ELECTROCARDIOGRAM T WAVE	2 (2.3%)	[3]	1 (1.2%)	[1]	1 (1.2%)	[1]	>0.99	>0.99
INVERSION								
WEIGHT DECREASED	0		0		1 (1.2%)	[2]		0.494
BLOOD ALKALINE	1 (1.2%)	[1]	0		0		>0.99	>0.99
PHOSPHATASE INCREASED								
BLOOD CREATINE	1 (1.2%)	[2]	0		0		>0.99	>0.99
PHOSPHOKINASE INCREASED								
BLOOD URINE PRESENT	1 (1.2%)	[1]	0		0		>0.99	>0.99
BODY TEMPERATURE	0		1 (1.2%)	[1]	0		0.494	
INCREASED								
CYSTOSCOPY	1 (1.2%)	[1]	0		0		>0.99	>0.99

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	n(%)	[AEs]	n(%)	[AEs]	n(%)	[AEs]	Low Dose	High Dose
ELECTROCARDIOGRAM ST SEGMENT DEPRESSIO	4 (4.7%)	[4]	1 (1.2%)	[2]	0		0.368	0.121*
ELECTROCARDIOGRAM T WAVE AMPLITUDE DEC	1 (1.2%)	[1]	1 (1.2%)	[1]	0		>0.99	>0.99
HEART RATE INCREASED	1 (1.2%)	[2]	0		0		>0.99	>0.99
HEART RATE IRREGULAR	1 (1.2%)	[4]	0		0		>0.99	>0.99
NASAL MUCOSA BIOPSY	0		1 (1.2%)	[1]	0		0.494	
METABOLISM AND NUTRITION DISORDERS	6 (7.0%)	[8]	1 (1.2%)	[1]	2 (2.4%)	[4]	0.117*	0.278
DECREASED APPETITE	1 (1.2%)	[2]	0		1 (1.2%)	[2]	>0.99	>0.99
INCREASED APPETITE	1 (1.2%)	[2]	0		1 (1.2%)	[2]	>0.99	>0.99
DEHYDRATION	1 (1.2%)	[1]	0		0		>0.99	>0.99
DIABETES MELLITUS	1 (1.2%)	[1]	0		0		>0.99	>0.99
FOOD CRAVING	1 (1.2%)	[1]	1 (1.2%)	[1]	0		>0.99	>0.99
HYPONATRAEMIA	1 (1.2%)	[1]	0		0		>0.99	>0.99
MUSCULOSKELETAL AND CONNECTIVE TISSUE DI	4 (4.7%)	[6]	7 (8.3%)	[10]	7 (8.3%)	[10]	0.367	0.367
BACK PAIN	1 (1.2%)	[2]	1 (1.2%)	[1]	3 (3.6%)	[4]	>0.99	0.365
ARTHRALGIA	1 (1.2%)	[1]	2 (2.4%)	[4]	1 (1.2%)	[1]	0.618	>0.99

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Table 14-5.01
Incidence of Treatment Emergent Adverse Events by Treatment Group

System Organ Class/ Preferred Term	Placebo (N=86)		Xanomeline Low (N=84)		Xanomeline High (N=84)		Fisher's Exact p-values Placebo vs. Low Dose vs. Placebo vs. High Dose	
	n(%)	[AEs]	n(%)	[AEs]	n(%)	[AEs]		
ARTHRITIS	0		0		1 (1.2%)	[1]		0.494
FLANK PAIN	0		0		1 (1.2%)	[1]		0.494
MUSCLE SPASMS	0		1 (1.2%)	[1]	1 (1.2%)	[2]	0.494	0.494
MYALGIA	0		0		1 (1.2%)	[1]		0.494
MUSCULAR WEAKNESS	0		1 (1.2%)	[2]	0		0.494	
PAIN IN EXTREMITY	1 (1.2%)	[1]	0		0		>0.99	>0.99
SHOULDER PAIN	1 (1.2%)	[2]	2 (2.4%)	[2]	0		0.618	>0.99
NEOPLASMS BENIGN, MALIGNANT AND UNSPECIF	0		2 (2.4%)	[3]	1 (1.2%)	[1]	0.243	0.494
PROSTATE CANCER	0		0		1 (1.2%)	[1]		0.494
COLON CANCER	0		1 (1.2%)	[1]	0		0.494	
MALIGNANT FIBROUS HISTIOCYTOMA	0		1 (1.2%)	[2]	0		0.494	
NERVOUS SYSTEM DISORDERS	8 (9.3%)	[11]	20 (23.8%)	[40]	25 (29.8%)	[41]	0.013*	0.001*
DIZZINESS	2 (2.3%)	[3]	8 (9.5%)	[13]	11 (13.1%)	[15]	0.056*	0.009*
HEADACHE	3 (3.5%)	[3]	3 (3.6%)	[4]	5 (6.0%)	[8]	>0.99	0.493
SYNCOPE	0		4 (4.8%)	[6]	3 (3.6%)	[4]	0.058*	0.118*
BURNING SENSATION	0		0		2 (2.4%)	[2]		0.243
AMNESIA	0		0		1 (1.2%)	[2]		0.494

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	n(%)	[AEs]	n(%)	[AEs]	n(%)	[AEs]		
COGNITIVE DISORDER	0		0		1 (1.2%)	[1]		0.494
HYPERSOMNIA	0		0		1 (1.2%)	[1]		0.494
LETHARGY	0		1 (1.2%)	[1]	1 (1.2%)	[1]	0.494	0.494
PARAESTHESIA	0		0		1 (1.2%)	[1]		0.494
PAROSMIA	0		0		1 (1.2%)	[2]		0.494
PARTIAL SEIZURES WITH SECONDARY GENERA	0		0		1 (1.2%)	[1]		0.494
SOMNOLENCE	2 (2.3%)	[3]	3 (3.6%)	[5]	1 (1.2%)	[1]	0.68	>0.99
SYNCOPE VASOVAGAL	0		0		1 (1.2%)	[1]		0.494
TRANSIENT ISCHAEMIC ATTACK	0		2 (2.4%)	[3]	1 (1.2%)	[1]	0.243	0.494
BALANCE DISORDER	0		1 (1.2%)	[3]	0		0.494	
COMPLEX PARTIAL SEIZURES	0		1 (1.2%)	[1]	0		0.494	
COORDINATION ABNORMAL	0		1 (1.2%)	[1]	0		0.494	
HEMIANOPIA HOMONYMOUS	0		1 (1.2%)	[1]	0		0.494	
PARAESTHESIA ORAL	0		1 (1.2%)	[1]	0		0.494	
PARKINSON'S DISEASE	1 (1.2%)	[1]	0		0		>0.99	>0.99
PSYCHOMOTOR HYPERACTIVITY	1 (1.2%)	[1]	0		0		>0.99	>0.99
STUPOR	0		1 (1.2%)	[1]	0		0.494	
PSYCHIATRIC DISORDERS	10 (11.6%)	[12]	10 (11.9%)	[14]	8 (9.5%)	[11]	>0.99	0.804

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System Organ Class/ Preferred Term	Placebo (N=86)		Xanomeline Low (N=84)		Xanomeline High (N=84)		Fisher's Exact p-values Placebo vs. Placebo vs. High Dose	
	n(%)	[AEs]	n(%)	[AEs]	n(%)	[AEs]	Low Dose	High Dose
INSOMNIA	2 (2.3%)	[3]	0		2 (2.4%)	[2]	0.497	>0.99
AGITATION	2 (2.3%)	[2]	2 (2.4%)	[2]	1 (1.2%)	[1]	>0.99	>0.99
CONFUSIONAL STATE	2 (2.3%)	[2]	3 (3.6%)	[3]	1 (1.2%)	[1]	0.68	>0.99
DELIRIUM	0		0		1 (1.2%)	[1]		0.494
DELUSION	1 (1.2%)	[1]	0		1 (1.2%)	[1]	>0.99	>0.99
HALLUCINATION	0		0		1 (1.2%)	[1]		0.494
HALLUCINATION, VISUAL	0		0		1 (1.2%)	[1]		0.494
LIBIDO DECREASED	0		0		1 (1.2%)	[1]		0.494
LISTLESS	0		0		1 (1.2%)	[1]		0.494
NIGHTMARE	0		0		1 (1.2%)	[1]		0.494
ANXIETY	0		3 (3.6%)	[4]	0		0.118*	
COMPLETED SUICIDE	1 (1.2%)	[1]	0		0		>0.99	>0.99
DEPRESSED MOOD	0		1 (1.2%)	[2]	0		0.494	
DISORIENTATION	1 (1.2%)	[1]	0		0		>0.99	>0.99
IRRITABILITY	1 (1.2%)	[2]	1 (1.2%)	[1]	0		>0.99	>0.99
RESTLESSNESS	0		1 (1.2%)	[2]	0		0.494	
RENAL AND URINARY DISORDERS	4 (4.7%)	[5]	3 (3.6%)	[3]	3 (3.6%)	[4]	>0.99	>0.99
CALCULUS URETHRAL	0		0		1 (1.2%)	[1]		0.494
MICTURITION URGENCY	1 (1.2%)	[1]	1 (1.2%)	[1]	1 (1.2%)	[2]	>0.99	>0.99
NEPHROLITHIASIS	1 (1.2%)	[1]	0		1 (1.2%)	[1]	>0.99	>0.99

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System Organ Class/ Preferred Term	Placebo (N=86)		Xanomeline Low (N=84)		Xanomeline High (N=84)		Fisher's Exact p-values Placebo vs. Low Dose vs. Placebo vs. High Dose	
	n(%)	[AEs]	n(%)	[AEs]	n(%)	[AEs]	Low Dose	High Dose
DYSURIA	1 (1.2%)	[1]	1 (1.2%)	[1]	0		>0.99	>0.99
INCONTINENCE	0		1 (1.2%)	[1]	0		0.494	
POLLAKEIURIA	1 (1.2%)	[2]	0		0		>0.99	>0.99
REPRODUCTIVE SYSTEM AND BREAST DISORDERS	2 (2.3%)	[4]	0		1 (1.2%)	[1]	0.497	>0.99
BENIGN PROSTATIC HYPERPLASIA	1 (1.2%)	[2]	0		1 (1.2%)	[1]	>0.99	>0.99
PELVIC PAIN	1 (1.2%)	[2]	0		0		>0.99	>0.99
RESPIRATORY, THORACIC AND MEDIASTINAL DI	8 (9.3%)	[12]	9 (10.7%)	[14]	10 (11.9%)	[22]	0.803	0.626
COUGH	1 (1.2%)	[1]	5 (6.0%)	[7]	5 (6.0%)	[7]	0.115*	0.115*
NASAL CONGESTION	3 (3.5%)	[3]	1 (1.2%)	[1]	3 (3.6%)	[4]	0.621	>0.99
EPISTAXIS	0		1 (1.2%)	[1]	2 (2.4%)	[2]	0.494	0.243
ALLERGIC GRANULOMATOUS ANGIITIS	0		0		1 (1.2%)	[1]		0.494
DYSPNOEA	1 (1.2%)	[1]	1 (1.2%)	[1]	1 (1.2%)	[1]	>0.99	>0.99
PHARYNGEAL ERYTHEMA	0		0		1 (1.2%)	[2]		0.494
PHARYNGOLARYNGEAL PAIN	0		1 (1.2%)	[1]	1 (1.2%)	[1]	0.494	0.494
PRODUCTIVE COUGH	0		0		1 (1.2%)	[1]		0.494

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	n(%)	[AEs]	n(%)	[AEs]	n(%)	[AEs]	Low Dose	High Dose
RESPIRATORY TRACT CONGESTION	0		0		1 (1.2%)	[1]		0.494
RHINORRHOEA	0		1 (1.2%)	[2]	1 (1.2%)	[2]	0.494	0.494
DYSPHONIA	0		1 (1.2%)	[1]	0		0.494	
EMPHYSEMA	1 (1.2%)	[1]	0		0		>0.99	>0.99
HAEMOPTYSIS	1 (1.2%)	[2]	0		0		>0.99	>0.99
POSTNASAL DRIP	1 (1.2%)	[2]	0		0		>0.99	>0.99
RALES	1 (1.2%)	[2]	0		0		>0.99	>0.99
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	20 (23.3%)	[45]	39 (46.4%)	[111]	40 (47.6%)	[104]	0.002*	0.001*
PRURITUS	8 (9.3%)	[11]	21 (25.0%)	[31]	26 (31.0%)	[38]	0.008*	0.000*
ERYTHEMA	8 (9.3%)	[12]	14 (16.7%)	[22]	14 (16.7%)	[22]	0.175	0.175
RASH	5 (5.8%)	[9]	13 (15.5%)	[18]	9 (10.7%)	[15]	0.048*	0.277
HYPERHIDROSIS	2 (2.3%)	[2]	4 (4.8%)	[5]	8 (9.5%)	[10]	0.441	0.056*
SKIN IRRITATION	3 (3.5%)	[4]	6 (7.1%)	[13]	5 (6.0%)	[8]	0.326	0.493
RASH PRURITIC	0		1 (1.2%)	[2]	2 (2.4%)	[3]	0.494	0.243
ACTINIC KERATOSIS	0		0		1 (1.2%)	[1]		0.494
BLISTER	0		5 (6.0%)	[8]	1 (1.2%)	[2]	0.028*	0.494
PRURITUS GENERALISED	0		1 (1.2%)	[4]	1 (1.2%)	[1]	0.494	0.494
RASH MACULO-PAPULAR	0		0		1 (1.2%)	[1]		0.494

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	n(%)	[AEs]	n(%)	[AEs]	n(%)	[AEs]		
SKIN ODOUR ABNORMAL	0		0		1 (1.2%)	[1]		0.494
URTICARIA	0		1 (1.2%)	[3]	1 (1.2%)	[2]	0.494	0.494
ALOPECIA	1 (1.2%)	[1]	0		0		>0.99	>0.99
COLD SWEAT	1 (1.2%)	[3]	0		0		>0.99	>0.99
DERMATITIS CONTACT	0		1 (1.2%)	[2]	0		0.494	
DRUG ERUPTION	1 (1.2%)	[1]	0		0		>0.99	>0.99
RASH ERYTHEMATOUS	0		1 (1.2%)	[1]	0		0.494	
SKIN EXFOLIATION	0		1 (1.2%)	[2]	0		0.494	
SKIN ULCER	1 (1.2%)	[2]	0		0		>0.99	>0.99
SOCIAL CIRCUMSTANCES	0		0		1 (1.2%)	[1]		0.494
ALCOHOL USE	0		0		1 (1.2%)	[1]		0.494
SURGICAL AND MEDICAL PROCEDURES	2 (2.3%)	[2]	1 (1.2%)	[1]	2 (2.4%)	[2]	>0.99	>0.99
ACROCHORDON EXCISION	0		0		1 (1.2%)	[1]		0.494
SKIN LESION EXCISION	0		0		1 (1.2%)	[1]		0.494
CATARACT OPERATION	1 (1.2%)	[1]	1 (1.2%)	[1]	0		>0.99	>0.99
EYE LASER SURGERY	1 (1.2%)	[1]	0		0		>0.99	>0.99
VASCULAR DISORDERS	3 (3.5%)	[7]	3 (3.6%)	[3]	1 (1.2%)	[1]	>0.99	0.621

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	n(%)	[AEs]	n(%)	[AEs]	n(%)	[AEs]	Low Dose	High Dose
WOUND HAEMORRHAGE	0		0		1 (1.2%)	[1]		0.494
HOT FLUSH	0		1 (1.2%)	[1]	0		0.494	
HYPERTENSION	1 (1.2%)	[2]	1 (1.2%)	[1]	0		>0.99	>0.99
HYPOTENSION	2 (2.3%)	[3]	1 (1.2%)	[1]	0		>0.99	0.497
ORTHOSTATIC HYPOTENSION	1 (1.2%)	[2]	0		0		>0.99	>0.99

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