

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

System Organ Class/ Preferred Term	n (%)	[AEs]	Placebo (N=86)	Xanomeline Low (N=84)	Xanomeline High (N=84)	Fisher's Exact p-values	
						Placebo vs. Low Dose	Placebo vs. High Dose
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=86)	[AES]	[AES]	Placebo vs. Low Dose	Placebo vs. High Dose
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 TACHYCARDIA	0		1 (1.2%) [2]		0	0.494	
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 SYNDROME	0		1 (1.2%) [2]		0	0.494	
CONGENITAL, FAMILIAL AND GENETIC DISORDERS	0		1 (1.2%) [1]	2 (2.4%) [2]	0.494	0.243	
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=86)			Placebo	vs. Placebo
							vs. 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	0			0	1 (1.2%) [1]		0.494
HAEMORRHAGE							
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]	Placebo vs. Low Dose	Placebo vs. High Dose
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 SITE	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=86)	[AES]	[AES]	Placebo vs. Low Dose	Placebo vs. High Dose
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=86)	[AES]	n (%)	[AES]	Placebo vs. Low Dose	Placebo vs. High Dose
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	
HEPATOBILIARY 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	6 (7.0%) [12]			1 (1.2%) [2]	3 (3.6%) [5]	0.117*	0.496	
INFECTION								
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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						Placebo vs. Low Dose	Placebo vs. High Dose
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=86)			Placebo vs. Low Dose	Placebo vs. High Dose
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
INCCREASED							
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
INCCREASED							
CYSTOSCOPY	1 (1.2%) [1]			0	0	>0.99	>0.99

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	n (%)	[AEs]	n (%)	[AEs]	n (%)	[AEs]	Placebo vs.	Placebo vs.	
							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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						Placebo vs. Low Dose	Placebo vs. High Dose
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	0			1 (1.2%) [2]	0	0.494	
HISTIOCYTOMA							
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

Note: Treatment emergent events are defined as events which start on or after the start of treatment.

Note: Adverse events are coded using MedDRA.

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Note: P-values are based on Fisher's Exact test for the comparison of placebo versus each active treatment group. An asterisk is appended to p-values that are less than 0.15.

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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	
		n (%)	[AES]	n (%)	[AES]	Placebo vs. Placebo	Low Dose vs. High Dose
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	0		0		1 (1.2%) [1]		0.494
SECONDARY GENERA							
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	0		2 (2.4%) [3]		1 (1.2%) [1]	0.243	0.494
ATTACK							
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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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		
	n (%)	[AEs]	n (%)	[AEs]	n (%)	[AEs]	Placebo	vs. Placebo	vs. 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	

Note: Treatment emergent events are defined as events which start on or after the start of treatment.

Note: Adverse events are coded using MedDRA.

Note: Percentages are based on the number of subjects in the safety population within each treatment group.

Note: P-values are based on Fisher's Exact test for the comparison of placebo versus each active treatment group. An asterisk is appended to p-values that are less than 0.15.

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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	
		n (%)	[AES]	n (%)	[AES]	n (%)	[AES]
DYSURIA	1 (1.2%) [1]	1 (1.2%) [1]	0	>0.99	>0.99		
INCONTINENCE	0	1 (1.2%) [1]	0	0.494			
POLLAKIURIA	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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Note: Adverse events are coded using MedDRA.

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

System Organ Class/ Preferred Term	n (%)	[AES]	Placebo (N=86)	Xanomeline Low (N=84)	Xanomeline High (N=84)	Fisher's Exact p-values	
						Placebo vs. Low Dose	Placebo vs. High Dose
RESPIRATORY TRACT	0			0	1 (1.2%) [1]		0.494
CONGESTION							
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	20 (23.3%) [45]			39 (46.4%) [111]	40 (47.6%) [104]	0.002*	0.001*
TISSUE DISORDERS							
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 MACULOPAPULAR	0			0	1 (1.2%) [1]		0.494

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

System Organ Class/ Preferred Term	n (%)	[AES]	Placebo (N=86)	Xanomeline Low (N=84)	Xanomeline High (N=84)	Fisher's Exact p-values	
						Placebo vs. Placebo	vs. High Dose
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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System Organ Class/ Preferred Term	Placebo (N=86)	Xanomeline Low (N=84)		Xanomeline High (N=84)		Fisher's Exact p-values	
		n (%)	[AEs]	n (%)	[AEs]	Placebo vs.	Placebo vs.
						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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