Table S-065 Summary of Treatment Emergent Adverse Events by Maximum Severity, System Organ Class and Preferred Term in 16-Week Double-blind Period in Combination with Insulin Therapy (PXL008-020; Safety Population)

System Organ Class Preferred Term Maximum Severity	Placebo + Insulin N = 107	Imeglimin 1000 mg bid + Insulin N = 108
Any TEAE		
Mild	45 (42.1%)	51 (47.2%)
Moderate	4 (3.7%)	6 (5.6%)
Severe	2 (1.9%)	0
Metabolism and nutrition disorders (代謝および栄養障害)		
Mild	18 (16.8%)	23 (21.3%)
Moderate	2 (1.9%)	0
Hypoglycaemia (低血糖)		
Mild	16 (15.0%)	23 (21.3%)
Moderate	1 (0.9%)	0
Hyperglycaemia (高血糖)		
Mild	2 (1.9%)	0
Moderate	1 (0.9%)	0
Infections and infestations (感染症および寄生虫症)		
Mild	14 (13.1%)	24 (22.2%)
Moderate	1 (0.9%)	0
Nasopharyngitis (上咽頭炎)		
Mild	8 (7.5%)	16 (14.8%)
Bronchitis (気管支炎)		
Mild	0	3 (2.8%)
Folliculitis (毛包炎)		
Mild	0	2 (1.9%)
Herpes zoster (帯状疱疹)		
Mild	0	2 (1.9%)
Tinea pedis (足部白癬)		
Mild	1 (0.9%)	1 (0.9%)
Asymptomatic bacteriuria (無症候性細菌尿)		
Mild	0	1 (0.9%)
Gastroenteritis (胃腸炎)		
Mild	1 (0.9%)	0
Gingivitis (歯肉炎)		
Mild	1 (0.9%)	0
Oral herpes (口腔ヘルペス)		
Mild	1 (0.9%)	0
Otitis externa (外耳炎)		
Mild	1 (0.9%)	0
Periodontitis (歯周炎)		
Mild	0	1 (0.9%)

System Organ Class Preferred Term Maximum Severity	Placebo + Insulin N = 107	Imeglimin 1000 mg bid + Insulin N = 108
Pneumonia (肺炎)		
Moderate	1 (0.9%)	0
Pulpitis dental (歯髄炎)		
Mild	1 (0.9%)	0
Gastrointestinal disorders (胃腸障害)		
Mild	6 (5.6%)	9 (8.3%)
Moderate	1 (0.9%)	1 (0.9%)
Constipation (便秘)		
Mild	1 (0.9%)	3 (2.8%)
Diarrhoea (下痢)		
Mild	2 (1.9%)	2 (1.9%)
Nausea (悪心)		
Mild	2 (1.9%)	1 (0.9%)
Moderate	0	1 (0.9%)
Abdominal discomfort (腹部不快感)		
Mild	1 (0.9%)	1 (0.9%)
Gastrooesophageal reflux disease (胃食道逆流性疾患)		
Mild	0	1 (0.9%)
Moderate	1 (0.9%)	0
Vomiting (嘔吐)		
Mild	1 (0.9%)	0
Moderate	0	1 (0.9%)
Abdominal distension (腹部膨満)		
Mild	0	1 (0.9%)
Colitis ulcerative (潰瘍性大腸炎)		
Mild	0	1 (0.9%)
Dental caries (齲歯)		
Mild	0	1 (0.9%)
Periodontal disease (歯周病)		
Mild	0	1 (0.9%)
Toothache (歯痛)		
Mild	0	1 (0.9%)
Musculoskeletal and connective tissue disorders (筋骨格系および結合組織障害)		
Mild	4 (3.7%)	9 (8.3%)
Muscle spasms (筋痙縮)		
Mild	2 (1.9%)	2 (1.9%)
Arthralgia (関節痛)		
Mild	0	2 (1.9%)
Back pain (背部痛)		
Mild	2 (1.9%)	0

System Organ Class Preferred Term Maximum Severity	Placebo + Insulin N = 107	Imeglimin 1000 mg bid + Insulin N = 108
Myofascitis (筋筋膜炎)		
Mild	0	1 (0.9%)
Neck pain (頚部痛)		
Mild	0	1 (0.9%)
Osteoarthritis (変形性関節症)		
Mild	0	1 (0.9%)
Pain in extremity (四肢痛)		
Mild	0	1 (0.9%)
Spinal osteoarthritis (変形性脊椎症)		
Mild	0	1 (0.9%)
Synovial cyst (滑液嚢腫)		
Mild	0	1 (0.9%)
Respiratory, thoracic and mediastinal disorders (呼吸器、胸郭および縦隔障害)		
Mild	6 (5.6%)	1 (0.9%)
Moderate	2 (1.9%)	1 (0.9%)
Asthma (喘息)		
Mild	2 (1.9%)	1 (0.9%)
Upper respiratory tract inflammation (上気道の炎症)		
Mild	1 (0.9%)	0
Moderate	1 (0.9%)	0
Allergic cough (アレルギー性咳嗽)		
Mild	1 (0.9%)	0
Cough (咳嗽)		
Mild	1 (0.9%)	0
Epistaxis (鼻出血)		
Moderate	1 (0.9%)	0
Pulmonary embolism (肺塞栓症)		
Moderate	0	1 (0.9%)
Sleep apnoea syndrome (睡眠時無呼吸症候群)		
Mild	1 (0.9%)	0
Nervous system disorders (神経系障害)		
Mild	4 (3.7%)	1 (0.9%)
Severe	2 (1.9%)	0
Dizziness (浮動性めまい)		
Mild	2 (1.9%)	1 (0.9%)
Severe	1 (0.9%)	0
Diabetic neuropathy (糖尿病性ニューロパチー)		
Mild	1 (0.9%)	0
Guillain-Barre syndrome (ギラン・バレー症候群)		
Severe	1 (0.9%)	0

System Organ Class Preferred Term Maximum Severity	Placebo + Insulin N = 107	Imeglimin 1000 mg bid + Insulin N = 108
Sciatica (坐骨神経痛)		
Mild	1 (0.9%)	0
Skin and subcutaneous tissue disorders (皮膚および皮下組織障害)		
Mild	2 (1.9%)	3 (2.8%)
Urticaria (蕁麻疹)		
Mild	0	2 (1.9%)
Papule (丘疹)		
Mild	1 (0.9%)	0
Pruritus (そう痒症)		
Mild	0	1 (0.9%)
Solar dermatitis (日光皮膚炎)		
Mild	1 (0.9%)	0
General disorders and administration site conditions (一般・全身障害および投与部位の状態)		
Mild	3 (2.8%)	1 (0.9%)
Pyrexia (発熱)		
Mild	3 (2.8%)	1 (0.9%)
Injury, poisoning and procedural complications (傷害、中毒および処置合併症)		
Mild	2 (1.9%)	1 (0.9%)
Moderate	0	1 (0.9%)
Contusion (挫傷)		
Mild	2 (1.9%)	0
Heat illness (熱中症)		
Mild	0	1 (0.9%)
Muscle strain (肉離れ)		
Moderate	0	1 (0.9%)
Vascular disorders (血管障害)		
Mild	0	1 (0.9%)
Moderate	0	2 (1.9%)
Hypertension (高血圧)		
Mild	0	1 (0.9%)
Peripheral arterial occlusive disease (末梢動脈閉塞性疾患)		
Moderate	0	1 (0.9%)
Venous thrombosis limb (四肢静脈血栓症)		
Moderate	0	1 (0.9%)
Eye disorders (眼障害)		

System Organ Class Preferred Term Maximum Severity	Placebo + Insulin N = 107	Imeglimin 1000 mg bid + Insulin N = 108
Moderate	0	2 (1.9%)
Angle closure glaucoma (閉塞隅角緑内障)		
Moderate	0	1 (0.9%)
Vitreous haemorrhage (硝子体出血)		
Moderate	0	1 (0.9%)
Cardiac disorders (心臓障害)		
Mild	1 (0.9%)	0
Bundle branch block right (右脚ブロック)		
Mild	1 (0.9%)	0
Ear and labyrinth disorders (耳および迷路障害)		
Mild	1 (0.9%)	0
Vertigo positional (頭位性回転性めまい)		
Mild	1 (0.9%)	0
Hepatobiliary disorders (肝胆道系障害)		
Mild	0	1 (0.9%)
Gallbladder polyp (胆嚢ポリープ)		
Mild	0	1 (0.9%)
Investigations (臨床検査)		
Mild	0	1 (0.9%)
Blood creatine phosphokinase increased (血中クレアチンホスホキナーゼ増加)		
Mild	0	1 (0.9%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps) (良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）)		
Mild	0	1 (0.9%)
Lipoma (脂肪腫)		
Mild	0	1 (0.9%)
Renal and urinary disorders (腎および尿路障害)		
Mild	0	1 (0.9%)
Haematuria (血尿)		
Mild	0	1 (0.9%)
Reproductive system and breast disorders (生殖系および乳房障害)		
Mild	1 (0.9%)	0
Amenorrhoea (無月経)		

System Organ Class Preferred Term Maximum Severity	Placebo + Insulin N = 107	Imeglimin 1000 mg bid + Insulin N = 108
Mild	1 (0.9%)	0

- Abbreviations: bid, Twice a day; AE, Adverse event; TEAE, Treatment Emergent AE
- All adverse events were coded using MedDRA dictionary version 20.1.
- Within each subject, multiple reports of adverse events mapped to a common System Organ Class and Preferred Term are counted only once by the maximum severity.
- Percentages are based on Population N.

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Table S-067 Summary of Treatment Emergent Adverse Events by Maximum Severity, System Organ Class and Preferred Term in 52-Week Long-term Period in Combination with Insulin Therapy (PXL008-020; Long-term Safety Population)

System Organ Class Preferred Term Maximum Severity	Placebo/Imeglimin + Insulin N = 101	Imeglimin/Imeglimin + Insulin N = 108	Imeglimin + Insulin Total N = 209
Any TEAE			
Mild	69 (68.3%)	80 (74.1%)	149 (71.3%)
Moderate	5 (5.0%)	11 (10.2%)	16 (7.7%)
Severe	3 (3.0%)	1 (0.9%)	4 (1.9%)
Infections and infestations (感染症および寄生虫症)			
Mild	29 (28.7%)	51 (47.2%)	80 (38.3%)
Moderate	1 (1.0%)	1 (0.9%)	2 (1.0%)
Nasopharyngitis (上咽頭炎)			
Mild	16 (15.8%)	36 (33.3%)	52 (24.9%)
Bronchitis (気管支炎)			
Mild	5 (5.0%)	4 (3.7%)	9 (4.3%)
Influenza (インフルエンザ)			
Mild	4 (4.0%)	5 (4.6%)	9 (4.3%)
Gastroenteritis (胃腸炎)			
Mild	3 (3.0%)	1 (0.9%)	4 (1.9%)
Moderate	1 (1.0%)	0	1 (0.5%)
Cystitis (膀胱炎)			
Mild	1 (1.0%)	3 (2.8%)	4 (1.9%)
Herpes zoster (帯状疱疹)			
Mild	1 (1.0%)	2 (1.9%)	3 (1.4%)
Periodontitis (歯周炎)			
Mild	1 (1.0%)	2 (1.9%)	3 (1.4%)
Conjunctivitis (結膜炎)			
Mild	2 (2.0%)	0	2 (1.0%)
Folliculitis (毛包炎)			
Mild	0	2 (1.9%)	2 (1.0%)
Hordeolum (麦粒腫)			
Mild	1 (1.0%)	1 (0.9%)	2 (1.0%)
Pharyngitis (咽頭炎)			
Mild	1 (1.0%)	1 (0.9%)	2 (1.0%)
Urinary tract infection (尿路感染)			
Mild	0	2 (1.9%)	2 (1.0%)
Asymptomatic bacteriuria (無症候性細菌尿)			
Mild	0	1 (0.9%)	1 (0.5%)
Erysipelas (丹毒)			
Moderate	0	1 (0.9%)	1 (0.5%)
Furuncle (せつ)			

System Organ Class Preferred Term Maximum Severity	Placebo/Imeglimin + Insulin N = 101	Imeglimin/Imeglimin + Insulin N = 108	Imeglimin + Insulin Total N = 209
Mild	0	1 (0.9%)	1 (0.5%)
Gastroenteritis viral (ウイルス性胃腸炎)			
Mild	1 (1.0%)	0	1 (0.5%)
Gingivitis (歯肉炎)			
Mild	0	1 (0.9%)	1 (0.5%)
Helicobacter infection (ヘリコバクター感染)			
Mild	1 (1.0%)	0	1 (0.5%)
Herpes simplex (単純ヘルペス)			
Mild	1 (1.0%)	0	1 (0.5%)
Oral herpes (口腔ヘルペス)			
Mild	1 (1.0%)	0	1 (0.5%)
Otitis media acute (急性中耳炎)			
Mild	1 (1.0%)	0	1 (0.5%)
Pneumonia mycoplasmal (マイコプラズマ性肺炎)			
Mild	1 (1.0%)	0	1 (0.5%)
Rhinitis (鼻炎)			
Mild	0	1 (0.9%)	1 (0.5%)
Sinusitis (副鼻腔炎)			
Mild	0	1 (0.9%)	1 (0.5%)
Soft tissue infection (軟部組織感染)			
Mild	0	1 (0.9%)	1 (0.5%)
Tinea pedis (足部白癬)			
Mild	0	1 (0.9%)	1 (0.5%)
Tonsillitis (扁桃炎)			
Mild	0	1 (0.9%)	1 (0.5%)
Upper respiratory tract infection (上気道感染)			
Mild	1 (1.0%)	0	1 (0.5%)
Metabolism and nutrition disorders (代謝および栄養障害)			
Mild	37 (36.6%)	42 (38.9%)	79 (37.8%)
Hypoglycaemia (低血糖)			
Mild	36 (35.6%)	39 (36.1%)	75 (35.9%)
Dyslipidaemia (脂質異常症)			
Mild	1 (1.0%)	1 (0.9%)	2 (1.0%)
Hyperglycaemia (高血糖)			
Mild	0	2 (1.9%)	2 (1.0%)
Hyponatraemia (低ナトリウム血症)			

System Organ Class Preferred Term Maximum Severity	Placebo/Imeglimin + Insulin N = 101	Imeglimin/Imeglimin + Insulin N = 108	Imeglimin + Insulin Total N = 209
Mild	1 (1.0%)	0	1 (0.5%)
Musculoskeletal and connective tissue disorders (筋骨格系および結合組織障害)			
Mild	8 (7.9%)	22 (20.4%)	30 (14.4%)
Moderate	1 (1.0%)	2 (1.9%)	3 (1.4%)
Back pain (背部痛)			
Mild	1 (1.0%)	4 (3.7%)	5 (2.4%)
Moderate	0	2 (1.9%)	2 (1.0%)
Muscle spasms (筋痙縮)			
Mild	1 (1.0%)	4 (3.7%)	5 (2.4%)
Arthralgia (関節痛)			
Mild	1 (1.0%)	3 (2.8%)	4 (1.9%)
Spinal osteoarthritis (変形性脊椎症)			
Mild	0	4 (3.7%)	4 (1.9%)
Musculoskeletal stiffness (筋骨格硬直)			
Mild	1 (1.0%)	1 (0.9%)	2 (1.0%)
Osteoarthritis (変形性関節症)			
Mild	0	2 (1.9%)	2 (1.0%)
Synovial cyst (滑液嚢腫)			
Mild	0	2 (1.9%)	2 (1.0%)
Tenosynovitis (腱鞘炎)			
Mild	1 (1.0%)	1 (0.9%)	2 (1.0%)
Trigger finger (弾発指)			
Mild	1 (1.0%)	1 (0.9%)	2 (1.0%)
Chondrocalcinosis pyrophosphate (ピロリン酸カルシウム結晶性軟骨石灰化症)			
Moderate	1 (1.0%)	0	1 (0.5%)
Intervertebral disc protrusion (椎間板突出)			
Mild	0	1 (0.9%)	1 (0.5%)
Lumbar spinal stenosis (腰部脊柱管狭窄症)			
Mild	0	1 (0.9%)	1 (0.5%)
Musculoskeletal pain (筋骨格痛)			
Mild	1 (1.0%)	0	1 (0.5%)
Myofascitis (筋筋膜炎)			
Mild	0	1 (0.9%)	1 (0.5%)
Neck pain (頚部痛)			
Mild	0	1 (0.9%)	1 (0.5%)

System Organ Class Preferred Term Maximum Severity	Placebo/Imeglimin + Insulin N = 101	Imeglimin/Imeglimin + Insulin N = 108	Imeglimin + Insulin Total N = 209
Nodal osteoarthritis (結節性変形性関節症)			
Mild	0	1 (0.9%)	1 (0.5%)
Pain in extremity (四肢痛)			
Mild	0	1 (0.9%)	1 (0.5%)
Synovitis (滑膜炎)			
Mild	0	1 (0.9%)	1 (0.5%)
Temporomandibular joint syndrome (顎関節症候群)			
Mild	0	1 (0.9%)	1 (0.5%)
Tendonitis (腱炎)			
Mild	1 (1.0%)	0	1 (0.5%)
Gastrointestinal disorders (胃腸障害)			
Mild	10 (9.9%)	19 (17.6%)	29 (13.9%)
Moderate	0	1 (0.9%)	1 (0.5%)
Constipation (便秘)			
Mild	0	6 (5.6%)	6 (2.9%)
Gastrooesophageal reflux disease (胃食道逆流性疾患)			
Mild	2 (2.0%)	3 (2.8%)	5 (2.4%)
Nausea (悪心)			
Mild	2 (2.0%)	2 (1.9%)	4 (1.9%)
Moderate	0	1 (0.9%)	1 (0.5%)
Abdominal discomfort (腹部不快感)			
Mild	1 (1.0%)	3 (2.8%)	4 (1.9%)
Diarrhoea (下痢)			
Mild	2 (2.0%)	2 (1.9%)	4 (1.9%)
Toothache (歯痛)			
Mild	2 (2.0%)	1 (0.9%)	3 (1.4%)
Abdominal pain upper (上腹部痛)			
Mild	0	2 (1.9%)	2 (1.0%)
Chronic gastritis (慢性胃炎)			
Mild	2 (2.0%)	0	2 (1.0%)
Dental caries (齲歯)			
Mild	1 (1.0%)	1 (0.9%)	2 (1.0%)
Gastritis (胃炎)			
Mild	1 (1.0%)	1 (0.9%)	2 (1.0%)
Periodontal disease (歯周病)			
Mild	0	2 (1.9%)	2 (1.0%)
Vomiting (嘔吐)			
Mild	1 (1.0%)	0	1 (0.5%)

System Organ Class Preferred Term Maximum Severity	Placebo/Imeglimin + Insulin N = 101	Imeglimin/Imeglimin + Insulin N = 108	Imeglimin + Insulin Total N = 209
Moderate	0	1 (0.9%)	1 (0.5%)
Abdominal distension (腹部膨満)			
Mild	0	1 (0.9%)	1 (0.5%)
Colitis ulcerative (潰瘍性大腸炎)			
Mild	0	1 (0.9%)	1 (0.5%)
Large intestine polyp (大腸ポリープ)			
Mild	1 (1.0%)	0	1 (0.5%)
Eye disorders (眼障害)			
Mild	6 (5.9%)	7 (6.5%)	13 (6.2%)
Moderate	0	3 (2.8%)	3 (1.4%)
Cataract (白内障)			
Mild	1 (1.0%)	2 (1.9%)	3 (1.4%)
Diabetic retinopathy (糖尿病網膜症)			
Mild	2 (2.0%)	1 (0.9%)	3 (1.4%)
Ocular hypertension (高眼圧症)			
Mild	0	2 (1.9%)	2 (1.0%)
Vitreous haemorrhage (硝子体出血)			
Mild	0	1 (0.9%)	1 (0.5%)
Moderate	0	1 (0.9%)	1 (0.5%)
Accommodation disorder (調節障害)			
Mild	1 (1.0%)	0	1 (0.5%)
Angle closure glaucoma (閉塞隅角緑内障)			
Moderate	0	1 (0.9%)	1 (0.5%)
Conjunctival hyperaemia (結膜充血)			
Mild	1 (1.0%)	0	1 (0.5%)
Conjunctivitis allergic (アレルギー性結膜炎)			
Mild	0	1 (0.9%)	1 (0.5%)
Diabetic retinal oedema (糖尿病性網膜浮腫)			
Moderate	0	1 (0.9%)	1 (0.5%)
Dry eye (眼乾燥)			
Mild	0	1 (0.9%)	1 (0.5%)
Glaucoma (緑内障)			
Mild	1 (1.0%)	0	1 (0.5%)
Macular oedema (黄斑浮腫)			
Mild	1 (1.0%)	0	1 (0.5%)
Pingueculitis (瞼裂斑炎)			
Mild	1 (1.0%)	0	1 (0.5%)
Retinal detachment (網膜剥離)			

System Organ Class Preferred Term Maximum Severity	Placebo/Imeglimin + Insulin N = 101	Imeglimin/Imeglimin + Insulin N = 108	Imeglimin + Insulin Total N = 209
Moderate	0	1 (0.9%)	1 (0.5%)
Retinal haemorrhage (網膜出血)			
Mild	0	1 (0.9%)	1 (0.5%)
Trichiasis (睫毛乱生)			
Mild	0	1 (0.9%)	1 (0.5%)
Nervous system disorders (神経系障害)			
Mild	5 (5.0%)	6 (5.6%)	11 (5.3%)
Moderate	1 (1.0%)	1 (0.9%)	2 (1.0%)
Severe	0	1 (0.9%)	1 (0.5%)
Headache (頭痛)			
Mild	3 (3.0%)	3 (2.8%)	6 (2.9%)
Dizziness (浮動性めまい)			
Mild	0	1 (0.9%)	1 (0.5%)
Moderate	1 (1.0%)	0	1 (0.5%)
Autonomic nervous system imbalance (自律神経失調)			
Mild	1 (1.0%)	0	1 (0.5%)
Carpal tunnel syndrome (手根管症候群)			
Mild	1 (1.0%)	0	1 (0.5%)
Epilepsy (てんかん)			
Moderate	0	1 (0.9%)	1 (0.5%)
Facial paralysis (顔面麻痺)			
Mild	0	1 (0.9%)	1 (0.5%)
Sciatica (坐骨神経痛)			
Severe	0	1 (0.9%)	1 (0.5%)
Somnolence (傾眠)			
Mild	0	1 (0.9%)	1 (0.5%)
Syncope (失神)			
Mild	1 (1.0%)	0	1 (0.5%)
Skin and subcutaneous tissue disorders (皮膚および皮下組織障害)			
Mild	2 (2.0%)	11 (10.2%)	13 (6.2%)
Dermatitis (皮膚炎)			
Mild	1 (1.0%)	2 (1.9%)	3 (1.4%)
Eczema (湿疹)			
Mild	0	2 (1.9%)	2 (1.0%)
Urticaria (蕁麻疹)			
Mild	0	2 (1.9%)	2 (1.0%)
Acne (ざ瘡)			
Mild	0	1 (0.9%)	1 (0.5%)

System Organ Class Preferred Term Maximum Severity	Placebo/Imeglimin + Insulin N = 101	Imeglimin/Imeglimin + Insulin N = 108	Imeglimin + Insulin Total N = 209
Cold sweat (冷汗)			
Mild	0	1 (0.9%)	1 (0.5%)
Drug eruption (薬疹)			
Mild	0	1 (0.9%)	1 (0.5%)
Hand dermatitis (手皮膚炎)			
Mild	1 (1.0%)	0	1 (0.5%)
Hyperkeratosis (過角化)			
Mild	0	1 (0.9%)	1 (0.5%)
Miliaria (汗疹)			
Mild	0	1 (0.9%)	1 (0.5%)
Pruritus (そう痒症)			
Mild	0	1 (0.9%)	1 (0.5%)
Respiratory, thoracic and mediastinal disorders (呼吸器、胸郭および縦隔障害)			
Mild	7 (6.9%)	3 (2.8%)	10 (4.8%)
Moderate	0	1 (0.9%)	1 (0.5%)
Upper respiratory tract inflammation (上気道の炎症)			
Mild	3 (3.0%)	1 (0.9%)	4 (1.9%)
Asthma (喘息)			
Mild	1 (1.0%)	1 (0.9%)	2 (1.0%)
Cough (咳嗽)			
Mild	1 (1.0%)	1 (0.9%)	2 (1.0%)
Sputum increased (喀痰増加)			
Mild	2 (2.0%)	0	2 (1.0%)
Pulmonary embolism (肺塞栓症)			
Moderate	0	1 (0.9%)	1 (0.5%)
Rhinitis allergic (アレルギー性鼻炎)			
Mild	1 (1.0%)	0	1 (0.5%)
Injury, poisoning and procedural complications (傷害、中毒および処置合併症)			
Mild	2 (2.0%)	7 (6.5%)	9 (4.3%)
Moderate	0	1 (0.9%)	1 (0.5%)
Contusion (挫傷)			
Mild	0	3 (2.8%)	3 (1.4%)
Stress fracture (ストレス骨折)			
Mild	0	2 (1.9%)	2 (1.0%)
Clavicle fracture (鎖骨骨折)			
Mild	1 (1.0%)	0	1 (0.5%)
Hand fracture (手骨折)			

System Organ Class Preferred Term Maximum Severity	Placebo/Imeglimin + Insulin N = 101	Imeglimin/Imeglimin + Insulin N = 108	Imeglimin + Insulin Total N = 209
Mild	0	1 (0.9%)	1 (0.5%)
Heat illness (熱中症)			
Mild	0	1 (0.9%)	1 (0.5%)
Ligament sprain (靱帯捻挫)			
Mild	0	1 (0.9%)	1 (0.5%)
Muscle strain (肉離れ)			
Moderate	0	1 (0.9%)	1 (0.5%)
Scratch (引っかき傷)			
Mild	1 (1.0%)	0	1 (0.5%)
Vascular disorders (血管障害)			
Mild	2 (2.0%)	5 (4.6%)	7 (3.3%)
Moderate	0	2 (1.9%)	2 (1.0%)
Hypertension (高血圧)			
Mild	2 (2.0%)	5 (4.6%)	7 (3.3%)
Peripheral arterial occlusive disease (末梢動脈閉塞性疾患)			
Moderate	0	1 (0.9%)	1 (0.5%)
Venous thrombosis limb (四肢静脈血栓症)			
Moderate	0	1 (0.9%)	1 (0.5%)
Investigations (臨床検査)			
Mild	1 (1.0%)	6 (5.6%)	7 (3.3%)
Blood creatine phosphokinase increased (血中クレアチンホスホキナーゼ増加)			
Mild	1 (1.0%)	2 (1.9%)	3 (1.4%)
Aspartate aminotransferase increased (アスパラギン酸アミノトランスフェラーゼ増加)			
Mild	0	1 (0.9%)	1 (0.5%)
Blood alkaline phosphatase increased (血中アルカリホスファターゼ増加)			
Mild	0	1 (0.9%)	1 (0.5%)
Blood glucose abnormal (血中ブドウ糖異常)			
Mild	0	1 (0.9%)	1 (0.5%)
Blood lactic acid increased (血中乳酸増加)			
Mild	0	1 (0.9%)	1 (0.5%)

System Organ Class Preferred Term Maximum Severity	Placebo/Imeglimin + Insulin N = 101	Imeglimin/Imeglimin + Insulin N = 108	Imeglimin + Insulin Total N = 209
Neoplasms benign, malignant and unspecified (incl cysts and polyps) (良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）)			
Mild	1 (1.0%)	3 (2.8%)	4 (1.9%)
Moderate	2 (2.0%)	0	2 (1.0%)
Severe	1 (1.0%)	0	1 (0.5%)
Papillary thyroid cancer (乳頭様甲状腺癌)			
Moderate	2 (2.0%)	0	2 (1.0%)
Benign neoplasm of thyroid gland (甲状腺の良性新生物)			
Mild	0	1 (0.9%)	1 (0.5%)
Intraductal papillary mucinous neoplasm (膵管内乳頭粘液性腫瘍)			
Mild	1 (1.0%)	0	1 (0.5%)
Lipoma (脂肪腫)			
Mild	0	1 (0.9%)	1 (0.5%)
Pancreatic carcinoma (膵癌)			
Severe	1 (1.0%)	0	1 (0.5%)
Uterine leiomyoma (子宮平滑筋腫)			
Mild	0	1 (0.9%)	1 (0.5%)
General disorders and administration site conditions (一般・全身障害および投与部位の状態)			
Mild	2 (2.0%)	3 (2.8%)	5 (2.4%)
Severe	1 (1.0%)	0	1 (0.5%)
Pyrexia (発熱)			
Mild	2 (2.0%)	2 (1.9%)	4 (1.9%)
Oedema peripheral (末梢性浮腫)			
Mild	0	1 (0.9%)	1 (0.5%)
Sudden death (突然死)			
Severe	1 (1.0%)	0	1 (0.5%)
Hepatobiliary disorders (肝胆道系障害)			
Mild	2 (2.0%)	2 (1.9%)	4 (1.9%)
Severe	1 (1.0%)	0	1 (0.5%)
Hepatic steatosis (脂肪肝)			
Mild	1 (1.0%)	1 (0.9%)	2 (1.0%)
Gallbladder polyp (胆嚢ポリープ)			
Mild	0	1 (0.9%)	1 (0.5%)

System Organ Class Preferred Term Maximum Severity	Placebo/Imeglimin + Insulin N = 101	Imeglimin/Imeglimin + Insulin N = 108	Imeglimin + Insulin Total N = 209
Hepatic function abnormal (肝機能異常)			
Severe	1 (1.0%)	0	1 (0.5%)
Hyperplastic cholecystopathy (過形成性胆嚢症)			
Mild	1 (1.0%)	0	1 (0.5%)
Immune system disorders (免疫系障害)			
Mild	1 (1.0%)	4 (3.7%)	5 (2.4%)
Seasonal allergy (季節性アレルギー)			
Mild	1 (1.0%)	4 (3.7%)	5 (2.4%)
Ear and labyrinth disorders (耳および迷路障害)			
Mild	1 (1.0%)	3 (2.8%)	4 (1.9%)
Meniere's disease (メニエール病)			
Mild	1 (1.0%)	0	1 (0.5%)
Tinnitus (耳鳴)			
Mild	0	1 (0.9%)	1 (0.5%)
Vertigo (回転性めまい)			
Mild	0	1 (0.9%)	1 (0.5%)
Vertigo positional (頭位性回転性めまい)			
Mild	0	1 (0.9%)	1 (0.5%)
Cardiac disorders (心臓障害)			
Mild	1 (1.0%)	0	1 (0.5%)
Moderate	1 (1.0%)	1 (0.9%)	2 (1.0%)
Atrial fibrillation (心房細動)			
Mild	1 (1.0%)	0	1 (0.5%)
Cardiac failure congestive (うっ血性心不全)			
Moderate	1 (1.0%)	0	1 (0.5%)
Coronary artery stenosis (冠動脈狭窄)			
Moderate	0	1 (0.9%)	1 (0.5%)
Extrasystoles (期外収縮)			
Mild	1 (1.0%)	0	1 (0.5%)
Reproductive system and breast disorders (生殖系および乳房障害)			
Mild	2 (2.0%)	1 (0.9%)	3 (1.4%)

System Organ Class Preferred Term Maximum Severity	Placebo/Imeglimin + Insulin N = 101	Imeglimin/Imeglimin + Insulin N = 108	Imeglimin + Insulin Total N = 209
Benign prostatic hyperplasia (良性前立腺肥大症)			
Mild	1 (1.0%)	1 (0.9%)	2 (1.0%)
Prostatomegaly (前立腺腫大)			
Mild	1 (1.0%)	0	1 (0.5%)
Psychiatric disorders (精神障害)			
Mild	1 (1.0%)	1 (0.9%)	2 (1.0%)
Depressive symptom (抑うつ症状)			
Mild	1 (1.0%)	0	1 (0.5%)
Insomnia (不眠症)			
Mild	0	1 (0.9%)	1 (0.5%)
Renal and urinary disorders (腎および尿路障害)			
Mild	1 (1.0%)	1 (0.9%)	2 (1.0%)
Haematuria (血尿)			
Mild	0	1 (0.9%)	1 (0.5%)
Renal cyst (腎嚢胞)			
Mild	1 (1.0%)	0	1 (0.5%)
Blood and lymphatic system disorders (血液およびリンパ系障害)			
Mild	1 (1.0%)	0	1 (0.5%)
Iron deficiency anaemia (鉄欠乏性貧血)			
Mild	1 (1.0%)	0	1 (0.5%)

- Abbreviations: AE, Adverse event; TEAE, Treatment Emergent AE
- All adverse events were coded using MedDRA dictionary version 20.1.
- "Imeglimin" in this table means "Imeglimin 1000 mg twice daily".
- The Long-term Safety Population excludes data during administration of placebo in the double-blind period.
- "Imeglimin + Insulin Total" is the sum of subjects in the placebo group in the open-label period and Imeglimin group in the double-blind and open-label periods.
- Within each subject, multiple reports of adverse events mapped to a common System Organ Class and Preferred Term are counted only once by the maximum severity.
- Percentages are based on Population N.

Control No:<<t-s-067-aesev-020lt.sas, 2020-03-06T00:08:05>>

Table S-068 Summary of Treatment Emergent Adverse Events (Incidence >= 2%) by Timing of Initial Onset, System Organ Class and Preferred Term in 24-Week Double-blind Period with Monotherapy (PXL008-014, PXL008-018; Safety Population)

System Organ Class Preferred Term Time Period	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
Number of patients in each period					
Week 1 to 4	182	75	180	75	330
Week 5 to 8	181	75	179	70	324
Week 9 to 12	178	74	177	69	320
Week 13 to 16	173	72	174	68	314
Week 17 to 20	168	72	171	68	311
Week 21 or later	168	71	171	67	309
Any TEAE					
Week 1 to 4	25 (13.7%)	12 (16.0%)	25 (13.9%)	24 (32.0%)	61 (18.5%)
Week 5 to 8	19 (10.5%)	12 (16.0%)	20 (11.2%)	10 (14.3%)	42 (13.0%)
Week 9 to 12	21 (11.8%)	8 (10.8%)	13 (7.3%)	5 (7.2%)	26 (8.1%)
Week 13 to 16	13 (7.5%)	5 (6.9%)	10 (5.7%)	2 (2.9%)	17 (5.4%)
Week 17 to 20	9 (5.4%)	8 (11.1%)	13 (7.6%)	8 (11.8%)	29 (9.3%)
Week 21 or later	12 (7.1%)	6 (8.5%)	12 (7.0%)	6 (9.0%)	24 (7.8%)
Infections and infestations (感染症および寄生虫症)					
Nasopharyngitis (上咽頭炎)					
Week 1 to 4	5 (2.7%)	2 (2.7%)	4 (2.2%)	3 (4.0%)	9 (2.7%)
Week 5 to 8	3 (1.7%)	3 (4.0%)	3 (1.7%)	3 (4.3%)	9 (2.8%)
Week 9 to 12	3 (1.7%)	3 (4.1%)	3 (1.7%)	4 (5.8%)	10 (3.1%)
Week 13 to 16	2 (1.2%)	2 (2.8%)	7 (4.0%)	0	9 (2.9%)
Week 17 to 20	3 (1.8%)	2 (2.8%)	6 (3.5%)	3 (4.4%)	11 (3.5%)
Week 21 or later	4 (2.4%)	8 (11.3%)	10 (5.8%)	5 (7.5%)	23 (7.4%)
Bronchitis (気管支炎)					
Week 1 to 4	0	1 (1.3%)	1 (0.6%)	1 (1.3%)	3 (0.9%)
Week 5 to 8	1 (0.6%)	0	0	0	0
Week 9 to 12	0	2 (2.7%)	1 (0.6%)	0	3 (0.9%)
Week 13 to 16	0	0	0	0	0
Week 17 to 20	0	0	0	0	0
Week 21 or later	0	0	0	0	0
Gastroenteritis (胃腸炎)					
Week 1 to 4	1 (0.5%)	0	0	0	0
Week 5 to 8	0	0	0	0	0
Week 9 to 12	0	0	0	0	0
Week 13 to 16	0	1 (1.4%)	0	0	1 (0.3%)
Week 17 to 20	0	1 (1.4%)	2 (1.2%)	0	3 (1.0%)
Week 21 or later	1 (0.6%)	0	0	0	0
Cystitis (膀胱炎)					
Week 1 to 4	0	0	0	0	0
Week 5 to 8	1 (0.6%)	0	0	0	0
Week 9 to 12	0	2 (2.7%)	0	0	2 (0.6%)
Week 13 to 16	0	0	0	0	0

System Organ Class Preferred Term Time Period	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
Week 17 to 20	0	0	0	0	0
Week 21 or later	0	0	0	0	0
Gastrointestinal disorders (胃腸障害)					
Diarrhoea (下痢)					
Week 1 to 4	0	0	3 (1.7%)	5 (6.7%)	8 (2.4%)
Week 5 to 8	0	1 (1.3%)	1 (0.6%)	1 (1.4%)	3 (0.9%)
Week 9 to 12	1 (0.6%)	0	1 (0.6%)	0	1 (0.3%)
Week 13 to 16	0	0	0	0	0
Week 17 to 20	0	1 (1.4%)	0	0	1 (0.3%)
Week 21 or later	0	1 (1.4%)	0	0	1 (0.3%)
Abdominal discomfort (腹部不快感)					
Week 1 to 4	0	0	1 (0.6%)	3 (4.0%)	4 (1.2%)
Week 5 to 8	0	1 (1.3%)	1 (0.6%)	2 (2.9%)	4 (1.2%)
Week 9 to 12	0	0	1 (0.6%)	1 (1.4%)	2 (0.6%)
Week 13 to 16	0	0	0	0	0
Week 17 to 20	0	0	0	0	0
Week 21 or later	0	0	0	1 (1.5%)	1 (0.3%)
Vomiting (嘔吐)					
Week 1 to 4	0	0	1 (0.6%)	3 (4.0%)	4 (1.2%)
Week 5 to 8	0	0	0	0	0
Week 9 to 12	2 (1.1%)	0	0	0	0
Week 13 to 16	1 (0.6%)	0	0	0	0
Week 17 to 20	0	0	0	1 (1.5%)	1 (0.3%)
Week 21 or later	1 (0.6%)	0	0	0	0
Nausea (悪心)					
Week 1 to 4	1 (0.5%)	0	1 (0.6%)	3 (4.0%)	4 (1.2%)
Week 5 to 8	0	1 (1.3%)	0	1 (1.4%)	2 (0.6%)
Week 9 to 12	0	0	0	0	0
Week 13 to 16	0	0	0	0	0
Week 17 to 20	0	0	0	1 (1.5%)	1 (0.3%)
Week 21 or later	0	0	0	0	0
Dental caries (齲歯)					
Week 1 to 4	2 (1.1%)	0	1 (0.6%)	0	1 (0.3%)
Week 5 to 8	0	0	1 (0.6%)	0	1 (0.3%)
Week 9 to 12	1 (0.6%)	0	0	0	0
Week 13 to 16	0	0	0	0	0
Week 17 to 20	0	0	0	1 (1.5%)	1 (0.3%)
Week 21 or later	1 (0.6%)	0	0	0	0
Abdominal pain upper (上腹部痛)					
Week 1 to 4	0	0	0	0	0
Week 5 to 8	1 (0.6%)	0	0	0	0
Week 9 to 12	0	0	0	0	0
Week 13 to 16	0	0	0	0	0
Week 17 to 20	0	0	0	0	0
Week 21 or later	0	2 (2.8%)	1 (0.6%)	0	3 (1.0%)

System Organ Class Preferred Term Time Period	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
Metabolism and nutrition disorders (代謝および栄養障害)					
Hyperglycaemia (高血糖)					
Week 1 to 4	2 (1.1%)	0	0	0	0
Week 5 to 8	2 (1.1%)	2 (2.7%)	0	0	2 (0.6%)
Week 9 to 12	3 (1.7%)	0	0	0	0
Week 13 to 16	3 (1.7%)	0	1 (0.6%)	0	1 (0.3%)
Week 17 to 20	3 (1.8%)	0	0	0	0
Week 21 or later	3 (1.8%)	1 (1.4%)	0	1 (1.5%)	2 (0.6%)
Hypoglycaemia (低血糖)					
Week 1 to 4	2 (1.1%)	1 (1.3%)	4 (2.2%)	1 (1.3%)	6 (1.8%)
Week 5 to 8	0	2 (2.7%)	1 (0.6%)	1 (1.4%)	4 (1.2%)
Week 9 to 12	0	0	0	1 (1.4%)	1 (0.3%)
Week 13 to 16	0	0	0	0	0
Week 17 to 20	0	1 (1.4%)	0	1 (1.5%)	2 (0.6%)
Week 21 or later	0	1 (1.4%)	0	0	1 (0.3%)
Musculoskeletal and connective tissue disorders (筋骨格系および結合組織障害)					
Arthralgia (関節痛)					
Week 1 to 4	0	0	0	1 (1.3%)	1 (0.3%)
Week 5 to 8	2 (1.1%)	0	1 (0.6%)	0	1 (0.3%)
Week 9 to 12	1 (0.6%)	0	0	0	0
Week 13 to 16	1 (0.6%)	0	0	0	0
Week 17 to 20	0	1 (1.4%)	0	0	1 (0.3%)
Week 21 or later	0	0	0	0	0
Back pain (背部痛)					
Week 1 to 4	0	0	0	0	0
Week 5 to 8	0	0	0	1 (1.4%)	1 (0.3%)
Week 9 to 12	0	2 (2.7%)	0	0	2 (0.6%)
Week 13 to 16	0	1 (1.4%)	0	0	1 (0.3%)
Week 17 to 20	0	1 (1.4%)	1 (0.6%)	0	2 (0.6%)
Week 21 or later	0	0	0	0	0
Nervous system disorders (神経系障害)					
Dizziness (浮動性めまい)					
Week 1 to 4	1 (0.5%)	0	1 (0.6%)	0	1 (0.3%)
Week 5 to 8	0	0	0	0	0
Week 9 to 12	3 (1.7%)	1 (1.4%)	0	0	1 (0.3%)
Week 13 to 16	0	0	0	0	0
Week 17 to 20	0	0	0	0	0
Week 21 or later	0	0	0	0	0
Headache (頭痛)					
Week 1 to 4	0	0	0	0	0
Week 5 to 8	0	1 (1.3%)	1 (0.6%)	0	2 (0.6%)
Week 9 to 12	1 (0.6%)	0	0	0	0

System Organ Class Preferred Term Time Period	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
Week 13 to 16	1 (0.6%)	0	0	0	0
Week 17 to 20	0	0	0	0	0
Week 21 or later	0	1 (1.4%)	0	0	1 (0.3%)
Injury, poisoning and procedural complications (傷害、中毒および処置合併症)					
Contusion (挫傷)					
Week 1 to 4	0	0	0	0	0
Week 5 to 8	1 (0.6%)	0	0	0	0
Week 9 to 12	0	0	1 (0.6%)	0	1 (0.3%)
Week 13 to 16	0	1 (1.4%)	0	0	1 (0.3%)
Week 17 to 20	0	1 (1.4%)	0	0	1 (0.3%)
Week 21 or later	0	0	0	1 (1.5%)	1 (0.3%)
Arthropod sting (節足動物刺傷)					
Week 1 to 4	0	0	0	0	0
Week 5 to 8	0	1 (1.3%)	0	0	1 (0.3%)
Week 9 to 12	0	0	0	0	0
Week 13 to 16	0	1 (1.4%)	0	1 (1.5%)	2 (0.6%)
Week 17 to 20	0	0	0	1 (1.5%)	1 (0.3%)
Week 21 or later	0	0	0	0	0
Skin and subcutaneous tissue disorders (皮膚および皮下組織障害)					
Eczema (湿疹)					
Week 1 to 4	0	1 (1.3%)	1 (0.6%)	0	2 (0.6%)
Week 5 to 8	2 (1.1%)	0	0	0	0
Week 9 to 12	0	0	0	2 (2.9%)	2 (0.6%)
Week 13 to 16	0	0	1 (0.6%)	0	1 (0.3%)
Week 17 to 20	0	1 (1.4%)	0	0	1 (0.3%)
Week 21 or later	0	0	0	1 (1.5%)	1 (0.3%)
Investigations (臨床検査)					
Culture urine positive (尿培養陽性)					
Week 1 to 4	0	0	0	0	0
Week 5 to 8	0	0	0	0	0
Week 9 to 12	0	0	0	0	0
Week 13 to 16	0	0	0	0	0
Week 17 to 20	0	1 (1.4%)	0	1 (1.5%)	2 (0.6%)
Week 21 or later	1 (0.6%)	0	0	3 (4.5%)	3 (1.0%)
Vascular disorders (血管障害)					
Hypertension (高血圧)					
Week 1 to 4	0	1 (1.3%)	0	0	1 (0.3%)
Week 5 to 8	0	0	0	0	0
Week 9 to 12	1 (0.6%)	0	0	0	0

System Organ Class Preferred Term Time Period	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
Week 13 to 16	0	0	1 (0.6%)	0	1 (0.3%)
Week 17 to 20	0	0	0	1 (1.5%)	1 (0.3%)
Week 21 or later	1 (0.6%)	1 (1.4%)	0	0	1 (0.3%)
General disorders and administration site conditions (一般・全身障害および投与部位の状態)					
Fatigue (疲労)					
Week 1 to 4	0	0	0	0	0
Week 5 to 8	0	0	1 (0.6%)	1 (1.4%)	2 (0.6%)
Week 9 to 12	1 (0.6%)	0	1 (0.6%)	1 (1.4%)	2 (0.6%)
Week 13 to 16	0	0	0	0	0
Week 17 to 20	0	0	0	0	0
Week 21 or later	0	0	0	0	0
Respiratory, thoracic and mediastinal disorders (呼吸器、胸郭および縦隔障害)					
Oropharyngeal pain (口腔咽頭痛)					
Week 1 to 4	0	0	0	1 (1.3%)	1 (0.3%)
Week 5 to 8	0	0	0	1 (1.4%)	1 (0.3%)
Week 9 to 12	1 (0.6%)	0	0	0	0
Week 13 to 16	0	0	0	0	0
Week 17 to 20	0	0	0	0	0
Week 21 or later	0	0	0	0	0
Rhinitis allergic (アレルギー性鼻炎)					
Week 1 to 4	0	0	0	0	0
Week 5 to 8	0	0	0	0	0
Week 9 to 12	0	0	0	0	0
Week 13 to 16	0	1 (1.4%)	0	0	1 (0.3%)
Week 17 to 20	0	0	0	0	0
Week 21 or later	0	1 (1.4%)	0	0	1 (0.3%)
Ear and labyrinth disorders (耳および迷路障害)					
Vertigo (回転性めまい)					
Week 1 to 4	0	0	0	0	0
Week 5 to 8	0	0	0	0	0
Week 9 to 12	0	0	0	1 (1.4%)	1 (0.3%)
Week 13 to 16	0	0	0	0	0
Week 17 to 20	0	0	1 (0.6%)	0	1 (0.3%)

System Organ Class Preferred Term Time Period	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
Week 21 or later	0	0	0	1 (1.5%)	1 (0.3%)

- Abbreviations: bid, Twice a day; AE, Adverse event; TEAE, Treatment Emergent AE
- All adverse events were coded using MedDRA dictionary version 20.1.
- Within each subject, multiple reports of adverse events mapped to a common System Organ Class and Preferred Term are counted only once.
- Number of patients in each period is defined as that of patients whose study duration was equal to or greater than the initial day of the corresponding time period.
- Percentages are based on "Number of patients in each period".
- Time Period: Week 1 to 4 = Day 1 to 28, Week 5 to 8 = Day 29 to 56, Week 9 to 12 = Day 57 to 84, Week 13 to 16 = Day 85 to 112, Week 17 to 20 = Day 113 to 140, Week 21 or later = Day 141 or later.

Control No:<<t-s-068-aeons-24wdb.sas, 2020-03-06T00:09:01>>

Table S-069 Summary of Treatment Emergent Adverse Events (Incidence >= 2%) by Timing of Every Onset, System Organ Class and Preferred Term in 24-Week Double-blind Period with Monotherapy (PXL008-014, PXL008-018; Safety Population)

System Organ Class Preferred Term Time Period	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
Number of patients in each period					
Week 1 to 4	182	75	180	75	330
Week 5 to 8	181	75	179	70	324
Week 9 to 12	178	74	177	69	320
Week 13 to 16	173	72	174	68	314
Week 17 to 20	168	72	171	68	311
Week 21 or later	168	71	171	67	309
Any TEAE					
Week 1 to 4	25 (13.7%)	12 (16.0%)	25 (13.9%)	24 (32.0%)	61 (18.5%)
Week 5 to 8	22 (12.2%)	15 (20.0%)	25 (14.0%)	14 (20.0%)	54 (16.7%)
Week 9 to 12	30 (16.9%)	14 (18.9%)	21 (11.9%)	17 (24.6%)	52 (16.3%)
Week 13 to 16	26 (15.0%)	8 (11.1%)	24 (13.8%)	6 (8.8%)	38 (12.1%)
Week 17 to 20	20 (11.9%)	14 (19.4%)	22 (12.9%)	19 (27.9%)	55 (17.7%)
Week 21 or later	24 (14.3%)	21 (29.6%)	29 (17.0%)	20 (29.9%)	70 (22.7%)
Infections and infestations (感染症および寄生虫症)					
Nasopharyngitis (上咽頭炎)					
Week 1 to 4	5 (2.7%)	2 (2.7%)	4 (2.2%)	3 (4.0%)	9 (2.7%)
Week 5 to 8	3 (1.7%)	4 (5.3%)	3 (1.7%)	3 (4.3%)	10 (3.1%)
Week 9 to 12	4 (2.2%)	3 (4.1%)	4 (2.3%)	5 (7.2%)	12 (3.8%)
Week 13 to 16	3 (1.7%)	2 (2.8%)	7 (4.0%)	1 (1.5%)	10 (3.2%)
Week 17 to 20	6 (3.6%)	3 (4.2%)	6 (3.5%)	4 (5.9%)	13 (4.2%)
Week 21 or later	6 (3.6%)	11 (15.5%)	14 (8.2%)	9 (13.4%)	34 (11.0%)
Bronchitis (気管支炎)					
Week 1 to 4	0	1 (1.3%)	1 (0.6%)	1 (1.3%)	3 (0.9%)
Week 5 to 8	1 (0.6%)	0	0	0	0
Week 9 to 12	0	2 (2.7%)	1 (0.6%)	0	3 (0.9%)
Week 13 to 16	0	0	0	0	0
Week 17 to 20	0	0	0	0	0
Week 21 or later	0	0	0	0	0
Gastroenteritis (胃腸炎)					
Week 1 to 4	1 (0.5%)	0	0	0	0
Week 5 to 8	0	0	0	0	0
Week 9 to 12	0	0	0	0	0
Week 13 to 16	0	1 (1.4%)	0	0	1 (0.3%)
Week 17 to 20	0	1 (1.4%)	2 (1.2%)	0	3 (1.0%)
Week 21 or later	1 (0.6%)	0	0	0	0
Cystitis (膀胱炎)					
Week 1 to 4	0	0	0	0	0
Week 5 to 8	1 (0.6%)	0	0	0	0
Week 9 to 12	0	2 (2.7%)	0	0	2 (0.6%)
Week 13 to 16	0	0	0	0	0

System Organ Class Preferred Term Time Period	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
Week 17 to 20	0	0	0	0	0
Week 21 or later	0	0	0	0	0
Gastrointestinal disorders (胃腸障害)					
Diarrhoea (下痢)					
Week 1 to 4	0	0	3 (1.7%)	5 (6.7%)	8 (2.4%)
Week 5 to 8	0	1 (1.3%)	1 (0.6%)	1 (1.4%)	3 (0.9%)
Week 9 to 12	1 (0.6%)	0	1 (0.6%)	0	1 (0.3%)
Week 13 to 16	0	0	0	0	0
Week 17 to 20	0	1 (1.4%)	0	0	1 (0.3%)
Week 21 or later	0	1 (1.4%)	0	0	1 (0.3%)
Abdominal discomfort (腹部不快感)					
Week 1 to 4	0	0	1 (0.6%)	3 (4.0%)	4 (1.2%)
Week 5 to 8	0	1 (1.3%)	1 (0.6%)	2 (2.9%)	4 (1.2%)
Week 9 to 12	0	0	1 (0.6%)	2 (2.9%)	3 (0.9%)
Week 13 to 16	0	0	0	0	0
Week 17 to 20	0	0	0	0	0
Week 21 or later	0	0	0	1 (1.5%)	1 (0.3%)
Vomiting (嘔吐)					
Week 1 to 4	0	0	1 (0.6%)	3 (4.0%)	4 (1.2%)
Week 5 to 8	0	0	0	0	0
Week 9 to 12	2 (1.1%)	0	0	1 (1.4%)	1 (0.3%)
Week 13 to 16	1 (0.6%)	0	0	0	0
Week 17 to 20	0	0	0	2 (2.9%)	2 (0.6%)
Week 21 or later	1 (0.6%)	0	0	0	0
Nausea (悪心)					
Week 1 to 4	1 (0.5%)	0	1 (0.6%)	3 (4.0%)	4 (1.2%)
Week 5 to 8	0	1 (1.3%)	0	1 (1.4%)	2 (0.6%)
Week 9 to 12	1 (0.6%)	0	0	0	0
Week 13 to 16	0	0	0	0	0
Week 17 to 20	0	0	0	1 (1.5%)	1 (0.3%)
Week 21 or later	0	0	0	0	0
Dental caries (齲歯)					
Week 1 to 4	2 (1.1%)	0	1 (0.6%)	0	1 (0.3%)
Week 5 to 8	0	0	1 (0.6%)	0	1 (0.3%)
Week 9 to 12	1 (0.6%)	0	0	0	0
Week 13 to 16	0	0	0	0	0
Week 17 to 20	0	0	0	1 (1.5%)	1 (0.3%)
Week 21 or later	1 (0.6%)	0	0	0	0
Abdominal pain upper (上腹部痛)					
Week 1 to 4	0	0	0	0	0
Week 5 to 8	1 (0.6%)	0	0	0	0
Week 9 to 12	0	0	0	0	0
Week 13 to 16	0	0	0	0	0
Week 17 to 20	0	0	0	0	0
Week 21 or later	0	2 (2.8%)	1 (0.6%)	0	3 (1.0%)

System Organ Class Preferred Term Time Period	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
Metabolism and nutrition disorders (代謝および栄養障害)					
Hyperglycaemia (高血糖)					
Week 1 to 4	2 (1.1%)	0	0	0	0
Week 5 to 8	2 (1.1%)	2 (2.7%)	0	0	2 (0.6%)
Week 9 to 12	3 (1.7%)	0	0	0	0
Week 13 to 16	3 (1.7%)	0	1 (0.6%)	0	1 (0.3%)
Week 17 to 20	3 (1.8%)	0	0	0	0
Week 21 or later	3 (1.8%)	1 (1.4%)	0	1 (1.5%)	2 (0.6%)
Hypoglycaemia (低血糖)					
Week 1 to 4	2 (1.1%)	1 (1.3%)	4 (2.2%)	1 (1.3%)	6 (1.8%)
Week 5 to 8	1 (0.6%)	2 (2.7%)	1 (0.6%)	1 (1.4%)	4 (1.2%)
Week 9 to 12	1 (0.6%)	0	0	2 (2.9%)	2 (0.6%)
Week 13 to 16	1 (0.6%)	0	2 (1.1%)	1 (1.5%)	3 (1.0%)
Week 17 to 20	0	1 (1.4%)	1 (0.6%)	1 (1.5%)	3 (1.0%)
Week 21 or later	0	1 (1.4%)	1 (0.6%)	0	2 (0.6%)
Musculoskeletal and connective tissue disorders (筋骨格系および結合組織障害)					
Arthralgia (関節痛)					
Week 1 to 4	0	0	0	1 (1.3%)	1 (0.3%)
Week 5 to 8	2 (1.1%)	0	1 (0.6%)	0	1 (0.3%)
Week 9 to 12	1 (0.6%)	0	0	0	0
Week 13 to 16	1 (0.6%)	0	0	0	0
Week 17 to 20	0	1 (1.4%)	0	0	1 (0.3%)
Week 21 or later	0	0	0	0	0
Back pain (背部痛)					
Week 1 to 4	0	0	0	0	0
Week 5 to 8	0	0	0	1 (1.4%)	1 (0.3%)
Week 9 to 12	0	2 (2.7%)	0	0	2 (0.6%)
Week 13 to 16	0	1 (1.4%)	0	0	1 (0.3%)
Week 17 to 20	0	1 (1.4%)	1 (0.6%)	0	2 (0.6%)
Week 21 or later	0	0	0	0	0
Nervous system disorders (神経系障害)					
Dizziness (浮動性めまい)					
Week 1 to 4	1 (0.5%)	0	1 (0.6%)	0	1 (0.3%)
Week 5 to 8	0	0	0	0	0
Week 9 to 12	3 (1.7%)	1 (1.4%)	0	0	1 (0.3%)
Week 13 to 16	0	0	0	0	0
Week 17 to 20	0	0	0	0	0
Week 21 or later	0	0	0	0	0
Headache (頭痛)					
Week 1 to 4	0	0	0	0	0
Week 5 to 8	0	1 (1.3%)	1 (0.6%)	0	2 (0.6%)

System Organ Class Preferred Term Time Period	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
Week 9 to 12	1 (0.6%)	0	0	0	0
Week 13 to 16	1 (0.6%)	0	0	0	0
Week 17 to 20	0	0	0	0	0
Week 21 or later	0	1 (1.4%)	0	0	1 (0.3%)
Injury, poisoning and procedural complications (傷害、中毒および処置合併症)					
Contusion (挫傷)					
Week 1 to 4	0	0	0	0	0
Week 5 to 8	1 (0.6%)	0	0	0	0
Week 9 to 12	0	0	1 (0.6%)	0	1 (0.3%)
Week 13 to 16	0	1 (1.4%)	0	0	1 (0.3%)
Week 17 to 20	0	1 (1.4%)	0	0	1 (0.3%)
Week 21 or later	0	0	0	1 (1.5%)	1 (0.3%)
Arthropod sting (節足動物刺傷)					
Week 1 to 4	0	0	0	0	0
Week 5 to 8	0	1 (1.3%)	0	0	1 (0.3%)
Week 9 to 12	0	0	0	0	0
Week 13 to 16	0	1 (1.4%)	0	1 (1.5%)	2 (0.6%)
Week 17 to 20	0	0	0	1 (1.5%)	1 (0.3%)
Week 21 or later	0	0	0	0	0
Skin and subcutaneous tissue disorders (皮膚および皮下組織障害)					
Eczema (湿疹)					
Week 1 to 4	0	1 (1.3%)	1 (0.6%)	0	2 (0.6%)
Week 5 to 8	2 (1.1%)	0	0	0	0
Week 9 to 12	0	0	0	2 (2.9%)	2 (0.6%)
Week 13 to 16	0	0	1 (0.6%)	0	1 (0.3%)
Week 17 to 20	0	1 (1.4%)	0	0	1 (0.3%)
Week 21 or later	0	0	0	1 (1.5%)	1 (0.3%)
Investigations (臨床検査)					
Culture urine positive (尿培養陽性)					
Week 1 to 4	0	0	0	0	0
Week 5 to 8	0	0	0	0	0
Week 9 to 12	0	0	0	0	0
Week 13 to 16	0	0	0	0	0
Week 17 to 20	0	1 (1.4%)	0	1 (1.5%)	2 (0.6%)
Week 21 or later	1 (0.6%)	1 (1.4%)	0	3 (4.5%)	4 (1.3%)
Vascular disorders (血管障害)					
Hypertension (高血圧)					
Week 1 to 4	0	1 (1.3%)	0	0	1 (0.3%)
Week 5 to 8	0	0	0	0	0

System Organ Class Preferred Term Time Period	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
Week 9 to 12	1 (0.6%)	0	0	0	0
Week 13 to 16	0	0	1 (0.6%)	0	1 (0.3%)
Week 17 to 20	0	0	0	1 (1.5%)	1 (0.3%)
Week 21 or later	1 (0.6%)	1 (1.4%)	0	0	1 (0.3%)
General disorders and administration site conditions (一般・全身障害および投与部位の状態)					
Fatigue (疲労)					
Week 1 to 4	0	0	0	0	0
Week 5 to 8	0	0	1 (0.6%)	1 (1.4%)	2 (0.6%)
Week 9 to 12	1 (0.6%)	0	1 (0.6%)	1 (1.4%)	2 (0.6%)
Week 13 to 16	0	0	0	0	0
Week 17 to 20	0	0	0	0	0
Week 21 or later	0	0	0	0	0
Respiratory, thoracic and mediastinal disorders (呼吸器、胸郭および縦隔障害)					
Oropharyngeal pain (口腔咽頭痛)					
Week 1 to 4	0	0	0	1 (1.3%)	1 (0.3%)
Week 5 to 8	0	0	0	1 (1.4%)	1 (0.3%)
Week 9 to 12	1 (0.6%)	0	0	0	0
Week 13 to 16	0	0	0	0	0
Week 17 to 20	0	0	0	0	0
Week 21 or later	0	0	0	0	0
Rhinitis allergic (アレルギー性鼻炎)					
Week 1 to 4	0	0	0	0	0
Week 5 to 8	0	0	0	0	0
Week 9 to 12	0	0	0	0	0
Week 13 to 16	0	1 (1.4%)	0	0	1 (0.3%)
Week 17 to 20	0	0	0	0	0
Week 21 or later	0	1 (1.4%)	0	0	1 (0.3%)
Ear and labyrinth disorders (耳および迷路障害)					
Vertigo (回転性めまい)					
Week 1 to 4	0	0	0	0	0
Week 5 to 8	0	0	0	0	0
Week 9 to 12	0	0	0	1 (1.4%)	1 (0.3%)
Week 13 to 16	0	0	0	0	0
Week 17 to 20	0	0	1 (0.6%)	0	1 (0.3%)

System Organ Class Preferred Term Time Period	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
Week 21 or later	0	0	0	1 (1.5%)	1 (0.3%)

- Abbreviations: bid, Twice a day; AE, Adverse event; TEAE, Treatment Emergent AE
- All adverse events were coded using MedDRA dictionary version 20.1.
- Within each subject and each period, multiple reports of adverse events mapped to a common System Organ Class and Preferred Term are counted only once.
- Number of patients in each period is defined as that of patients whose study duration was equal to or greater than the initial day of the corresponding time period.
- Percentages are based on "Number of patients in each period".
- Time Period: Week 1 to 4 = Day 1 to 28, Week 5 to 8 = Day 29 to 56, Week 9 to 12 = Day 57 to 84, Week 13 to 16 = Day 85 to 112, Week 17 to 20 = Day 113 to 140, Week 21 or later = Day 141 or later.

Control No:<<t-s-069-aeons-24wdb.sas, 2020-03-06T00:08:59>>

Table S-072 Summary of Treatment Emergent Adverse Events (Incidence >= 2%) by Timing of Initial Onset, System Organ Class and Preferred Term in 52-Week Long-term Period with Monotherapy and Combination Therapy (PXL008-019; Long-term Safety Population)

System Organ Class Preferred Term Time Period	Imeglimin N = 134	Imeglimin + SU N = 127	Imeglimin + GLIN N = 64	Imeglimin + BIG N = 64	Imeglimin + AGI N = 64	Imeglimin + TZD N = 65	Imeglimin + DPP4-I N = 63	Imeglimin + GLP1-RA N = 70	Imeglimin + SGLT2-I N = 63	Combination Total N = 580	Imeglimin Total N = 714
Number of patients in each period											
Week 1 to 4	134	127	64	64	64	65	63	70	63	580	714
Week 5 to 8	134	127	63	64	64	65	63	70	63	579	713
Week 9 to 16	133	126	63	64	64	65	62	69	63	576	709
Week 17 to 24	131	123	63	64	64	65	62	69	63	573	704
Week 25 to 32	130	123	63	63	64	65	61	69	63	571	701
Week 33 to 40	128	123	61	60	63	65	61	69	63	565	693
Week 41 to 48	128	119	60	60	62	65	60	69	63	558	686
Week 49 or later	127	116	60	58	62	65	60	67	62	550	677
Any TEAE											
Week 1 to 4	18 (13.4%)	25 (19.7%)	14 (21.9%)	20 (31.3%)	5 (7.8%)	15 (23.1%)	16 (25.4%)	16 (22.9%)	13 (20.6%)	124 (21.4%)	142 (19.9%)
Week 5 to 8	13 (9.7%)	14 (11.0%)	11 (17.5%)	4 (6.3%)	2 (3.1%)	9 (13.8%)	4 (6.3%)	12 (17.1%)	7 (11.1%)	63 (10.9%)	76 (10.7%)
Week 9 to 16	22 (16.5%)	22 (17.5%)	5 (7.9%)	7 (10.9%)	7 (10.9%)	7 (10.8%)	11 (17.7%)	11 (15.9%)	6 (9.5%)	76 (13.2%)	98 (13.8%)
Week 17 to 24	19 (14.5%)	12 (9.8%)	11 (17.5%)	5 (7.8%)	5 (7.8%)	4 (6.2%)	3 (4.8%)	5 (7.2%)	9 (14.3%)	54 (9.4%)	73 (10.4%)
Week 25 to 32	19 (14.6%)	15 (12.2%)	2 (3.2%)	5 (7.9%)	9 (14.1%)	8 (12.3%)	5 (8.2%)	6 (8.7%)	6 (9.5%)	56 (9.8%)	75 (10.7%)
Week 33 to 40	1 (0.8%)	7 (5.7%)	4 (6.6%)	4 (6.7%)	4 (6.3%)	4 (6.2%)	5 (8.2%)	2 (2.9%)	6 (9.5%)	36 (6.4%)	37 (5.3%)
Week 41 to 48	6 (4.7%)	5 (4.2%)	5 (8.3%)	1 (1.7%)	1 (1.6%)	2 (3.1%)	6 (10.0%)	3 (4.3%)	1 (1.6%)	24 (4.3%)	30 (4.4%)
Week 49 or later	0	2 (1.7%)	2 (3.3%)	2 (3.4%)	0	1 (1.5%)	0	1 (1.5%)	0	8 (1.5%)	8 (1.2%)
Infections and infestations (感染症および寄生虫症)											
Nasopharyngitis (上咽頭炎)											
Week 1 to 4	3 (2.2%)	4 (3.1%)	4 (6.3%)	0	0	4 (6.2%)	2 (3.2%)	4 (5.7%)	0	18 (3.1%)	21 (2.9%)
Week 5 to 8	4 (3.0%)	1 (0.8%)	2 (3.2%)	2 (3.1%)	0	1 (1.5%)	0	5 (7.1%)	2 (3.2%)	13 (2.2%)	17 (2.4%)
Week 9 to 16	5 (3.8%)	7 (5.6%)	3 (4.8%)	0	1 (1.6%)	3 (4.6%)	4 (6.5%)	3 (4.3%)	2 (3.2%)	23 (4.0%)	28 (3.9%)

System Organ Class Preferred Term Time Period	Imeglimin N = 134	Imeglimin + SU N = 127	Imeglimin + GLIN N = 64	Imeglimin + BIG N = 64	Imeglimin + AGI N = 64	Imeglimin + TZD N = 65	Imeglimin + DPP4-I N = 63	Imeglimin + GLP1-RA N = 70	Imeglimin + SGLT2-I N = 63	Combination Total N = 580	Imeglimin Total N = 714
Week 17 to 24	1 (0.8%)	6 (4.9%)	6 (9.5%)	2 (3.1%)	0	1 (1.5%)	0	1 (1.4%)	5 (7.9%)	21 (3.7%)	22 (3.1%)
Week 25 to 32	11 (8.5%)	10 (8.1%)	4 (6.3%)	2 (3.2%)	0	6 (9.2%)	4 (6.6%)	3 (4.3%)	4 (6.3%)	33 (5.8%)	44 (6.3%)
Week 33 to 40	5 (3.9%)	8 (6.5%)	4 (6.6%)	5 (8.3%)	3 (4.8%)	1 (1.5%)	3 (4.9%)	0	5 (7.9%)	29 (5.1%)	34 (4.9%)
Week 41 to 48	8 (6.3%)	1 (0.8%)	3 (5.0%)	5 (8.3%)	1 (1.6%)	1 (1.5%)	4 (6.7%)	2 (2.9%)	1 (1.6%)	18 (3.2%)	26 (3.8%)
Week 49 or later	3 (2.4%)	2 (1.7%)	1 (1.7%)	0	0	1 (1.5%)	2 (3.3%)	2 (3.0%)	1 (1.6%)	9 (1.6%)	12 (1.8%)
Pharyngitis (咽頭炎)											
Week 1 to 4	0	0	0	0	0	1 (1.5%)	1 (1.6%)	0	0	2 (0.3%)	2 (0.3%)
Week 5 to 8	0	2 (1.6%)	0	0	0	2 (3.1%)	0	0	0	4 (0.7%)	4 (0.6%)
Week 9 to 16	2 (1.5%)	1 (0.8%)	0	0	1 (1.6%)	0	0	0	1 (1.6%)	3 (0.5%)	5 (0.7%)
Week 17 to 24	3 (2.3%)	0	2 (3.2%)	0	1 (1.6%)	0	0	0	0	3 (0.5%)	6 (0.9%)
Week 25 to 32	2 (1.5%)	2 (1.6%)	0	0	0	0	0	0	2 (3.2%)	4 (0.7%)	6 (0.9%)
Week 33 to 40	0	0	0	0	0	0	1 (1.6%)	0	1 (1.6%)	2 (0.4%)	2 (0.3%)
Week 41 to 48	1 (0.8%)	0	1 (1.7%)	0	0	0	1 (1.7%)	1 (1.4%)	1 (1.6%)	4 (0.7%)	5 (0.7%)
Week 49 or later	0	0	1 (1.7%)	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Influenza (インフルエンザ)											
Week 1 to 4	0	0	0	0	0	0	0	0	1 (1.6%)	1 (0.2%)	1 (0.1%)
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	0	0	0	0	0	0	0	1 (1.4%)	0	1 (0.2%)	1 (0.1%)
Week 17 to 24	0	1 (0.8%)	0	0	1 (1.6%)	0	0	0	0	2 (0.3%)	2 (0.3%)
Week 25 to 32	0	1 (0.8%)	0	0	0	2 (3.1%)	0	0	0	3 (0.5%)	3 (0.4%)
Week 33 to 40	0	4 (3.3%)	1 (1.6%)	2 (3.3%)	0	0	1 (1.6%)	0	0	8 (1.4%)	8 (1.2%)
Week 41 to 48	4 (3.1%)	3 (2.5%)	0	3 (5.0%)	0	1 (1.5%)	0	0	1 (1.6%)	8 (1.4%)	12 (1.7%)
Week 49 or later	0	0	1 (1.7%)	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Bronchitis (気管支炎)											
Week 1 to 4	0	0	0	0	0	1 (1.5%)	0	0	0	1 (0.2%)	1 (0.1%)
Week 5 to 8	0	0	0	0	0	1 (1.5%)	0	0	0	1 (0.2%)	1 (0.1%)
Week 9 to 16	0	0	1 (1.6%)	1 (1.6%)	0	0	0	0	0	2 (0.3%)	2 (0.3%)
Week 17 to 24	0	0	0	0	0	0	0	0	0	0	0
Week 25 to 32	1 (0.8%)	1 (0.8%)	1 (1.6%)	1 (1.6%)	0	0	0	0	1 (1.6%)	4 (0.7%)	5 (0.7%)

System Organ Class Preferred Term Time Period	Imeglimin N = 134	Imeglimin + SU N = 127	Imeglimin + GLIN N = 64	Imeglimin + BIG N = 64	Imeglimin + AGI N = 64	Imeglimin + TZD N = 65	Imeglimin + DPP4-I N = 63	Imeglimin + GLP1-RA N = 70	Imeglimin + SGLT2-I N = 63	Combination Total N = 580	Imeglimin Total N = 714
Week 33 to 40	0	0	0	0	0	0	0	0	1 (1.6%)	1 (0.2%)	1 (0.1%)
Week 41 to 48	0	0	1 (1.7%)	0	0	1 (1.5%)	0	0	0	2 (0.4%)	2 (0.3%)
Week 49 or later	0	0	1 (1.7%)	0	0	1 (1.5%)	0	0	0	2 (0.4%)	2 (0.3%)
Gastroenteritis (胃腸炎)											
Week 1 to 4	1 (0.7%)	0	1 (1.6%)	0	0	0	0	0	0	1 (0.2%)	2 (0.3%)
Week 5 to 8	0	0	0	2 (3.1%)	0	0	0	0	0	2 (0.3%)	2 (0.3%)
Week 9 to 16	1 (0.8%)	0	0	1 (1.6%)	0	0	0	1 (1.4%)	0	2 (0.3%)	3 (0.4%)
Week 17 to 24	0	0	0	0	0	0	0	1 (1.4%)	0	1 (0.2%)	1 (0.1%)
Week 25 to 32	0	0	1 (1.6%)	0	0	1 (1.5%)	0	0	0	2 (0.4%)	2 (0.3%)
Week 33 to 40	0	0	0	0	0	0	0	0	0	0	0
Week 41 to 48	0	0	1 (1.7%)	0	1 (1.6%)	0	1 (1.7%)	0	1 (1.6%)	4 (0.7%)	4 (0.6%)
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Periodontitis (歯周炎)											
Week 1 to 4	0	0	0	1 (1.6%)	0	1 (1.5%)	1 (1.6%)	0	0	3 (0.5%)	3 (0.4%)
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	0	0	0	0	0	1 (1.5%)	0	0	0	1 (0.2%)	1 (0.1%)
Week 17 to 24	0	1 (0.8%)	0	1 (1.6%)	0	0	0	0	0	2 (0.3%)	2 (0.3%)
Week 25 to 32	0	1 (0.8%)	1 (1.6%)	0	0	0	1 (1.6%)	1 (1.4%)	0	4 (0.7%)	4 (0.6%)
Week 33 to 40	0	1 (0.8%)	0	0	0	1 (1.5%)	0	0	0	2 (0.4%)	2 (0.3%)
Week 41 to 48	0	0	0	0	0	0	0	0	0	0	0
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Cystitis (膀胱炎)											
Week 1 to 4	1 (0.7%)	0	0	0	0	0	0	0	0	0	1 (0.1%)
Week 5 to 8	0	1 (0.8%)	0	0	0	0	0	1 (1.4%)	0	2 (0.3%)	2 (0.3%)
Week 9 to 16	0	0	0	0	0	1 (1.5%)	0	1 (1.4%)	0	2 (0.3%)	2 (0.3%)
Week 17 to 24	0	1 (0.8%)	1 (1.6%)	0	0	0	0	0	1 (1.6%)	3 (0.5%)	3 (0.4%)
Week 25 to 32	0	0	1 (1.6%)	0	0	0	1 (1.6%)	0	0	2 (0.4%)	2 (0.3%)
Week 33 to 40	0	0	0	0	0	0	1 (1.6%)	0	0	1 (0.2%)	1 (0.1%)
Week 41 to 48	0	0	0	0	0	0	0	0	0	0	0

System Organ Class Preferred Term Time Period	Imeglimin N = 134	Imeglimin + SU N = 127	Imeglimin + GLIN N = 64	Imeglimin + BIG N = 64	Imeglimin + AGI N = 64	Imeglimin + TZD N = 65	Imeglimin + DPP4-I N = 63	Imeglimin + GLP1-RA N = 70	Imeglimin + SGLT2-I N = 63	Combination Total N = 580	Imeglimin Total N = 714
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Herpes zoster (帯状疱疹)											
Week 1 to 4	0	0	0	0	0	0	0	0	1 (1.6%)	1 (0.2%)	1 (0.1%)
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	0	1 (0.8%)	0	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 17 to 24	1 (0.8%)	0	0	0	0	0	0	0	1 (1.6%)	1 (0.2%)	2 (0.3%)
Week 25 to 32	0	0	0	0	0	1 (1.5%)	0	0	0	1 (0.2%)	1 (0.1%)
Week 33 to 40	1 (0.8%)	0	0	0	0	0	1 (1.6%)	1 (1.4%)	0	2 (0.4%)	3 (0.4%)
Week 41 to 48	0	0	0	0	0	0	0	0	0	0	0
Week 49 or later	0	0	1 (1.7%)	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Upper respiratory tract infection (上気道感染)											
Week 1 to 4	0	1 (0.8%)	0	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	1 (0.8%)	0	0	0	0	0	0	0	0	0	1 (0.1%)
Week 17 to 24	0	0	0	0	0	0	0	0	1 (1.6%)	1 (0.2%)	1 (0.1%)
Week 25 to 32	0	0	0	0	0	0	1 (1.6%)	0	0	1 (0.2%)	1 (0.1%)
Week 33 to 40	0	0	0	0	0	0	1 (1.6%)	0	0	1 (0.2%)	1 (0.1%)
Week 41 to 48	1 (0.8%)	0	0	0	0	0	0	0	0	0	1 (0.1%)
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Urinary tract infection (尿路感染)											
Week 1 to 4	0	0	0	0	0	0	0	0	0	0	0
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	0	0	0	0	0	2 (3.1%)	0	0	0	2 (0.3%)	2 (0.3%)
Week 17 to 24	0	0	0	0	0	0	0	0	0	0	0
Week 25 to 32	0	0	0	0	1 (1.6%)	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 33 to 40	0	0	0	0	1 (1.6%)	0	0	0	0	1 (0.2%)	1 (0.1%)

System Organ Class Preferred Term Time Period	Imeglimin N = 134	Imeglimin + SU N = 127	Imeglimin + GLIN N = 64	Imeglimin + BIG N = 64	Imeglimin + AGI N = 64	Imeglimin + TZD N = 65	Imeglimin + DPP4-I N = 63	Imeglimin + GLP1-RA N = 70	Imeglimin + SGLT2-I N = 63	Combination Total N = 580	Imeglimin Total N = 714
Week 41 to 48	0	0	0	0	1 (1.6%)	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Gingivitis (歯肉炎)											
Week 1 to 4	0	1 (0.8%)	0	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	0	0	0	0	0	0	0	1 (1.4%)	0	1 (0.2%)	1 (0.1%)
Week 17 to 24	0	0	0	0	0	0	0	0	0	0	0
Week 25 to 32	0	0	0	0	0	0	0	0	0	0	0
Week 33 to 40	0	0	0	0	0	0	0	0	0	0	0
Week 41 to 48	0	0	0	0	0	0	0	1 (1.4%)	0	1 (0.2%)	1 (0.1%)
Week 49 or later	0	0	0	0	0	1 (1.5%)	0	0	0	1 (0.2%)	1 (0.1%)
Pericoronitis (歯冠周囲炎)											
Week 1 to 4	0	0	0	0	0	0	0	0	0	0	0
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	0	0	0	0	1 (1.6%)	0	0	1 (1.4%)	0	2 (0.3%)	2 (0.3%)
Week 17 to 24	0	0	0	0	0	0	0	1 (1.4%)	0	1 (0.2%)	1 (0.1%)
Week 25 to 32	0	0	0	0	0	0	0	0	1 (1.6%)	1 (0.2%)	1 (0.1%)
Week 33 to 40	0	0	0	0	0	0	0	0	0	0	0
Week 41 to 48	0	0	0	0	0	0	0	0	0	0	0
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Gastrointestinal disorders (胃腸障害)											
Nausea (悪心)											
Week 1 to 4	3 (2.2%)	0	0	7 (10.9%)	0	1 (1.5%)	4 (6.3%)	3 (4.3%)	2 (3.2%)	17 (2.9%)	20 (2.8%)
Week 5 to 8	2 (1.5%)	0	0	0	0	0	0	0	1 (1.6%)	1 (0.2%)	3 (0.4%)
Week 9 to 16	0	1 (0.8%)	0	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 17 to 24	3 (2.3%)	0	0	0	0	0	0	0	0	0	3 (0.4%)

System Organ Class Preferred Term Time Period	Imeglimin N = 134	Imeglimin + SU N = 127	Imeglimin + GLIN N = 64	Imeglimin + BIG N = 64	Imeglimin + AGI N = 64	Imeglimin + TZD N = 65	Imeglimin + DPP4-I N = 63	Imeglimin + GLP1-RA N = 70	Imeglimin + SGLT2-I N = 63	Combination Total N = 580	Imeglimin Total N = 714
Week 25 to 32	0	0	0	1 (1.6%)	0	0	1 (1.6%)	0	1 (1.6%)	3 (0.5%)	3 (0.4%)
Week 33 to 40	0	0	0	0	0	0	0	0	0	0	0
Week 41 to 48	0	0	0	0	0	0	0	0	0	0	0
Week 49 or later	1 (0.8%)	0	0	0	1 (1.6%)	0	0	0	0	1 (0.2%)	2 (0.3%)
Diarrhoea (下痢)											
Week 1 to 4	2 (1.5%)	1 (0.8%)	3 (4.7%)	7 (10.9%)	0	2 (3.1%)	1 (1.6%)	1 (1.4%)	1 (1.6%)	16 (2.8%)	18 (2.5%)
Week 5 to 8	0	0	0	0	0	0	0	0	1 (1.6%)	1 (0.2%)	1 (0.1%)
Week 9 to 16	1 (0.8%)	0	0	3 (4.7%)	0	0	1 (1.6%)	0	0	4 (0.7%)	5 (0.7%)
Week 17 to 24	1 (0.8%)	2 (1.6%)	0	0	0	0	0	1 (1.4%)	0	3 (0.5%)	4 (0.6%)
Week 25 to 32	0	0	0	1 (1.6%)	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 33 to 40	0	0	0	0	0	0	0	0	0	0	0
Week 41 to 48	0	0	1 (1.7%)	0	0	0	0	1 (1.4%)	0	2 (0.4%)	2 (0.3%)
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Constipation (便秘)											
Week 1 to 4	3 (2.2%)	2 (1.6%)	1 (1.6%)	0	0	0	1 (1.6%)	0	0	4 (0.7%)	7 (1.0%)
Week 5 to 8	2 (1.5%)	0	0	1 (1.6%)	0	1 (1.5%)	1 (1.6%)	0	0	3 (0.5%)	5 (0.7%)
Week 9 to 16	0	4 (3.2%)	0	0	0	0	1 (1.6%)	0	2 (3.2%)	7 (1.2%)	7 (1.0%)
Week 17 to 24	0	1 (0.8%)	0	0	1 (1.6%)	0	1 (1.6%)	1 (1.4%)	0	4 (0.7%)	4 (0.6%)
Week 25 to 32	0	1 (0.8%)	0	0	0	0	1 (1.6%)	0	0	2 (0.4%)	2 (0.3%)
Week 33 to 40	0	0	0	0	1 (1.6%)	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 41 to 48	0	0	1 (1.7%)	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Gastrooesophageal reflux disease (胃食道逆流性疾患)											
Week 1 to 4	0	3 (2.4%)	0	0	0	0	0	0	0	3 (0.5%)	3 (0.4%)
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	0	0	0	1 (1.6%)	0	0	0	1 (1.4%)	0	2 (0.3%)	2 (0.3%)
Week 17 to 24	0	4 (3.3%)	1 (1.6%)	1 (1.6%)	0	0	0	0	0	6 (1.0%)	6 (0.9%)
Week 25 to 32	1 (0.8%)	0	0	0	0	0	0	0	0	0	1 (0.1%)

System Organ Class Preferred Term Time Period	Imeglimin N = 134	Imeglimin + SU N = 127	Imeglimin + GLIN N = 64	Imeglimin + BIG N = 64	Imeglimin + AGI N = 64	Imeglimin + TZD N = 65	Imeglimin + DPP4-I N = 63	Imeglimin + GLP1-RA N = 70	Imeglimin + SGLT2-I N = 63	Combination Total N = 580	Imeglimin Total N = 714
Week 33 to 40	2 (1.6%)	0	0	0	0	0	0	0	0	0	2 (0.3%)
Week 41 to 48	0	2 (1.7%)	0	0	0	0	0	0	0	2 (0.4%)	2 (0.3%)
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Abdominal pain upper (上腹部痛)											
Week 1 to 4	0	1 (0.8%)	0	2 (3.1%)	0	0	0	1 (1.4%)	0	4 (0.7%)	4 (0.6%)
Week 5 to 8	1 (0.7%)	0	0	0	0	0	0	0	0	0	1 (0.1%)
Week 9 to 16	0	0	0	0	0	0	0	0	0	0	0
Week 17 to 24	0	0	0	1 (1.6%)	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 25 to 32	1 (0.8%)	0	0	0	0	0	0	0	0	0	1 (0.1%)
Week 33 to 40	0	0	0	0	0	0	1 (1.6%)	0	0	1 (0.2%)	1 (0.1%)
Week 41 to 48	2 (1.6%)	0	1 (1.7%)	0	0	0	1 (1.7%)	0	0	2 (0.4%)	4 (0.6%)
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Dental caries (齲歯)											
Week 1 to 4	1 (0.7%)	0	0	0	0	1 (1.5%)	0	0	0	1 (0.2%)	2 (0.3%)
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	1 (0.8%)	0	1 (1.6%)	1 (1.6%)	0	0	1 (1.6%)	0	0	3 (0.5%)	4 (0.6%)
Week 17 to 24	1 (0.8%)	0	0	0	0	0	0	0	0	0	1 (0.1%)
Week 25 to 32	0	0	0	0	0	1 (1.5%)	0	0	0	1 (0.2%)	1 (0.1%)
Week 33 to 40	1 (0.8%)	0	0	0	0	0	1 (1.6%)	0	0	1 (0.2%)	2 (0.3%)
Week 41 to 48	1 (0.8%)	0	0	0	0	1 (1.5%)	0	0	0	1 (0.2%)	2 (0.3%)
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Vomiting (嘔吐)											
Week 1 to 4	0	0	0	3 (4.7%)	0	2 (3.1%)	1 (1.6%)	1 (1.4%)	0	7 (1.2%)	7 (1.0%)
Week 5 to 8	0	0	0	0	0	0	0	1 (1.4%)	0	1 (0.2%)	1 (0.1%)
Week 9 to 16	0	0	0	1 (1.6%)	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 17 to 24	1 (0.8%)	0	0	0	0	0	0	0	0	0	1 (0.1%)
Week 25 to 32	0	0	0	0	0	0	1 (1.6%)	0	0	1 (0.2%)	1 (0.1%)

System Organ Class Preferred Term Time Period	Imeglimin N = 134	Imeglimin + SU N = 127	Imeglimin + GLIN N = 64	Imeglimin + BIG N = 64	Imeglimin + AGI N = 64	Imeglimin + TZD N = 65	Imeglimin + DPP4-I N = 63	Imeglimin + GLP1-RA N = 70	Imeglimin + SGLT2-I N = 63	Combination Total N = 580	Imeglimin Total N = 714
Week 33 to 40	0	0	0	0	0	0	0	0	0	0	0
Week 41 to 48	0	0	0	0	0	0	0	0	0	0	0
Week 49 or later	0	0	0	0	0	0	0	0	1 (1.6%)	1 (0.2%)	1 (0.1%)
Abdominal discomfort (腹部不快感)											
Week 1 to 4	0	0	1 (1.6%)	3 (4.7%)	0	0	1 (1.6%)	0	0	5 (0.9%)	5 (0.7%)
Week 5 to 8	0	1 (0.8%)	0	0	1 (1.6%)	0	0	0	0	2 (0.3%)	2 (0.3%)
Week 9 to 16	0	1 (0.8%)	0	0	0	0	1 (1.6%)	0	0	2 (0.3%)	2 (0.3%)
Week 17 to 24	0	0	0	0	0	0	0	0	0	0	0
Week 25 to 32	0	0	0	0	0	0	0	0	0	0	0
Week 33 to 40	0	0	0	0	0	0	0	0	0	0	0
Week 41 to 48	0	0	0	0	0	0	0	0	0	0	0
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Chronic gastritis (慢性胃炎)											
Week 1 to 4	0	0	0	0	0	0	1 (1.6%)	0	0	1 (0.2%)	1 (0.1%)
Week 5 to 8	0	0	0	0	0	0	0	0	1 (1.6%)	1 (0.2%)	1 (0.1%)
Week 9 to 16	0	0	0	0	0	0	0	1 (1.4%)	0	1 (0.2%)	1 (0.1%)
Week 17 to 24	0	2 (1.6%)	0	1 (1.6%)	0	0	0	0	0	3 (0.5%)	3 (0.4%)
Week 25 to 32	0	0	0	0	0	0	1 (1.6%)	0	0	1 (0.2%)	1 (0.1%)
Week 33 to 40	0	0	0	0	0	0	0	0	0	0	0
Week 41 to 48	0	0	0	0	0	0	0	0	0	0	0
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Dyspepsia (消化不良)											
Week 1 to 4	0	0	0	0	0	0	1 (1.6%)	2 (2.9%)	0	3 (0.5%)	3 (0.4%)
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	0	1 (0.8%)	1 (1.6%)	0	0	0	0	0	0	2 (0.3%)	2 (0.3%)
Week 17 to 24	0	1 (0.8%)	0	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 25 to 32	0	0	0	0	0	0	1 (1.6%)	0	0	1 (0.2%)	1 (0.1%)

System Organ Class Preferred Term Time Period	Imeglimin N = 134	Imeglimin + SU N = 127	Imeglimin + GLIN N = 64	Imeglimin + BIG N = 64	Imeglimin + AGI N = 64	Imeglimin + TZD N = 65	Imeglimin + DPP4-I N = 63	Imeglimin + GLP1-RA N = 70	Imeglimin + SGLT2-I N = 63	Combination Total N = 580	Imeglimin Total N = 714
Week 33 to 40	0	0	0	0	0	0	0	0	0	0	0
Week 41 to 48	0	0	0	0	0	0	0	0	0	0	0
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Faeces soft (軟便)											
Week 1 to 4	1 (0.7%)	1 (0.8%)	0	1 (1.6%)	0	0	0	0	0	2 (0.3%)	3 (0.4%)
Week 5 to 8	0	0	0	0	0	0	0	0	1 (1.6%)	1 (0.2%)	1 (0.1%)
Week 9 to 16	0	0	0	1 (1.6%)	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 17 to 24	0	0	1 (1.6%)	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 25 to 32	0	0	0	0	0	0	0	0	0	0	0
Week 33 to 40	0	0	0	0	0	0	0	0	0	0	0
Week 41 to 48	0	0	0	0	0	0	0	0	0	0	0
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Large intestine polyp (大腸ポリープ)											
Week 1 to 4	0	0	0	0	0	0	0	0	1 (1.6%)	1 (0.2%)	1 (0.1%)
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	0	0	0	0	0	0	0	1 (1.4%)	0	1 (0.2%)	1 (0.1%)
Week 17 to 24	1 (0.8%)	0	0	0	0	0	1 (1.6%)	0	0	1 (0.2%)	2 (0.3%)
Week 25 to 32	0	0	0	1 (1.6%)	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 33 to 40	0	0	0	0	0	0	0	0	0	0	0
Week 41 to 48	0	0	0	1 (1.7%)	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Gastritis (胃炎)											
Week 1 to 4	0	0	0	0	1 (1.6%)	0	0	0	1 (1.6%)	2 (0.3%)	2 (0.3%)
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	0	0	0	0	0	0	0	0	0	0	0
Week 17 to 24	0	0	0	0	0	0	0	0	1 (1.6%)	1 (0.2%)	1 (0.1%)
Week 25 to 32	0	0	0	0	0	0	0	0	0	0	0

System Organ Class Preferred Term Time Period	Imeglimin N = 134	Imeglimin + SU N = 127	Imeglimin + GLIN N = 64	Imeglimin + BIG N = 64	Imeglimin + AGI N = 64	Imeglimin + TZD N = 65	Imeglimin + DPP4-I N = 63	Imeglimin + GLP1-RA N = 70	Imeglimin + SGLT2-I N = 63	Combination Total N = 580	Imeglimin Total N = 714
Week 33 to 40	0	0	0	0	0	0	0	1 (1.4%)	0	1 (0.2%)	1 (0.1%)
Week 41 to 48	0	0	0	0	0	0	0	0	0	0	0
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Abdominal distension (腹部膨満)											
Week 1 to 4	0	0	0	0	0	0	1 (1.6%)	0	1 (1.6%)	2 (0.3%)	2 (0.3%)
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	0	0	0	0	0	0	0	0	0	0	0
Week 17 to 24	0	0	0	0	0	0	0	0	0	0	0
Week 25 to 32	0	0	0	0	0	0	0	0	0	0	0
Week 33 to 40	0	0	0	0	0	0	0	0	1 (1.6%)	1 (0.2%)	1 (0.1%)
Week 41 to 48	0	0	0	0	0	0	0	0	0	0	0
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Metabolism and nutrition disorders (代謝および栄養障害)											
Hypoglycaemia (低血糖)											
Week 1 to 4	1 (0.7%)	5 (3.9%)	0	1 (1.6%)	0	0	0	0	0	6 (1.0%)	7 (1.0%)
Week 5 to 8	0	1 (0.8%)	2 (3.2%)	0	0	0	0	0	1 (1.6%)	4 (0.7%)	4 (0.6%)
Week 9 to 16	3 (2.3%)	4 (3.2%)	1 (1.6%)	0	0	0	2 (3.2%)	0	1 (1.6%)	8 (1.4%)	11 (1.6%)
Week 17 to 24	0	2 (1.6%)	2 (3.2%)	1 (1.6%)	1 (1.6%)	0	0	0	1 (1.6%)	7 (1.2%)	7 (1.0%)
Week 25 to 32	0	6 (4.9%)	2 (3.2%)	1 (1.6%)	1 (1.6%)	0	0	0	1 (1.6%)	11 (1.9%)	11 (1.6%)
Week 33 to 40	0	1 (0.8%)	0	0	0	2 (3.1%)	1 (1.6%)	2 (2.9%)	0	6 (1.1%)	6 (0.9%)
Week 41 to 48	1 (0.8%)	2 (1.7%)	2 (3.3%)	2 (3.3%)	0	0	2 (3.3%)	0	0	8 (1.4%)	9 (1.3%)
Week 49 or later	0	0	0	1 (1.7%)	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Hyperglycaemia (高血糖)											
Week 1 to 4	0	0	0	0	0	0	0	0	0	0	0
Week 5 to 8	0	1 (0.8%)	0	0	0	0	1 (1.6%)	2 (2.9%)	0	4 (0.7%)	4 (0.6%)

System Organ Class Preferred Term Time Period	Imeglimin N = 134	Imeglimin + SU N = 127	Imeglimin + GLIN N = 64	Imeglimin + BIG N = 64	Imeglimin + AGI N = 64	Imeglimin + TZD N = 65	Imeglimin + DPP4-I N = 63	Imeglimin + GLP1-RA N = 70	Imeglimin + SGLT2-I N = 63	Combination Total N = 580	Imeglimin Total N = 714
Week 9 to 16	0	1 (0.8%)	0	0	0	0	0	2 (2.9%)	0	3 (0.5%)	3 (0.4%)
Week 17 to 24	1 (0.8%)	1 (0.8%)	0	0	0	0	0	1 (1.4%)	1 (1.6%)	3 (0.5%)	4 (0.6%)
Week 25 to 32	0	1 (0.8%)	0	0	0	0	0	2 (2.9%)	0	3 (0.5%)	3 (0.4%)
Week 33 to 40	0	1 (0.8%)	0	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 41 to 48	2 (1.6%)	2 (1.7%)	0	0	1 (1.6%)	1 (1.5%)	0	1 (1.4%)	0	5 (0.9%)	7 (1.0%)
Week 49 or later	2 (1.6%)	0	0	0	0	0	1 (1.7%)	0	0	1 (0.2%)	3 (0.4%)
Decreased appetite (食欲減退)											
Week 1 to 4	0	0	0	0	0	1 (1.5%)	2 (3.2%)	0	0	3 (0.5%)	3 (0.4%)
Week 5 to 8	1 (0.7%)	0	0	1 (1.6%)	0	0	0	3 (4.3%)	1 (1.6%)	5 (0.9%)	6 (0.8%)
Week 9 to 16	1 (0.8%)	0	0	0	0	0	0	0	0	0	1 (0.1%)
Week 17 to 24	1 (0.8%)	0	0	1 (1.6%)	0	0	0	0	0	1 (0.2%)	2 (0.3%)
Week 25 to 32	0	0	0	0	0	0	0	0	0	0	0
Week 33 to 40	0	0	0	0	0	0	0	0	0	0	0
Week 41 to 48	0	0	0	0	0	0	0	0	0	0	0
Week 49 or later	0	0	0	0	0	1 (1.5%)	0	0	0	1 (0.2%)	1 (0.1%)
Musculoskeletal and connective tissue disorders (筋骨格系および結合組織障害)											
Back pain (背部痛)											
Week 1 to 4	0	0	0	0	0	0	0	0	0	0	0
Week 5 to 8	0	2 (1.6%)	1 (1.6%)	0	0	0	0	0	0	3 (0.5%)	3 (0.4%)
Week 9 to 16	1 (0.8%)	1 (0.8%)	1 (1.6%)	1 (1.6%)	0	0	1 (1.6%)	0	0	4 (0.7%)	5 (0.7%)
Week 17 to 24	1 (0.8%)	2 (1.6%)	0	0	2 (3.1%)	1 (1.5%)	0	0	0	5 (0.9%)	6 (0.9%)
Week 25 to 32	2 (1.5%)	2 (1.6%)	1 (1.6%)	0	0	2 (3.1%)	0	0	0	5 (0.9%)	7 (1.0%)
Week 33 to 40	0	1 (0.8%)	0	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 41 to 48	0	0	0	0	0	1 (1.5%)	0	0	0	1 (0.2%)	1 (0.1%)
Week 49 or later	1 (0.8%)	2 (1.7%)	0	0	0	0	0	0	0	2 (0.4%)	3 (0.4%)

System Organ Class Preferred Term Time Period	Imeglimin N = 134	Imeglimin + SU N = 127	Imeglimin + GLIN N = 64	Imeglimin + BIG N = 64	Imeglimin + AGI N = 64	Imeglimin + TZD N = 65	Imeglimin + DPP4-I N = 63	Imeglimin + GLP1-RA N = 70	Imeglimin + SGLT2-I N = 63	Combination Total N = 580	Imeglimin Total N = 714
Arthralgia (関節痛)											
Week 1 to 4	0	1 (0.8%)	0	1 (1.6%)	0	0	0	0	0	2 (0.3%)	2 (0.3%)
Week 5 to 8	1 (0.7%)	0	0	0	0	0	0	0	0	0	1 (0.1%)
Week 9 to 16	0	0	0	0	0	0	0	2 (2.9%)	0	2 (0.3%)	2 (0.3%)
Week 17 to 24	0	0	0	1 (1.6%)	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 25 to 32	0	0	0	0	0	0	1 (1.6%)	0	1 (1.6%)	2 (0.4%)	2 (0.3%)
Week 33 to 40	0	2 (1.6%)	0	0	0	1 (1.5%)	1 (1.6%)	0	0	4 (0.7%)	4 (0.6%)
Week 41 to 48	0	0	0	0	0	1 (1.5%)	0	0	0	1 (0.2%)	1 (0.1%)
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Pain in extremity (四肢痛)											
Week 1 to 4	0	0	1 (1.6%)	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	0	0	0	0	0	0	0	0	0	0	0
Week 17 to 24	1 (0.8%)	1 (0.8%)	1 (1.6%)	0	0	0	0	0	0	2 (0.3%)	3 (0.4%)
Week 25 to 32	0	2 (1.6%)	0	0	0	0	1 (1.6%)	0	0	3 (0.5%)	3 (0.4%)
Week 33 to 40	0	0	0	0	0	0	0	1 (1.4%)	0	1 (0.2%)	1 (0.1%)
Week 41 to 48	0	0	0	0	0	0	0	0	1 (1.6%)	1 (0.2%)	1 (0.1%)
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Myalgia (筋肉痛)											
Week 1 to 4	0	0	0	1 (1.6%)	0	0	0	0	1 (1.6%)	2 (0.3%)	2 (0.3%)
Week 5 to 8	0	1 (0.8%)	0	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 9 to 16	0	0	0	0	1 (1.6%)	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 17 to 24	0	0	0	0	0	0	0	0	0	0	0
Week 25 to 32	1 (0.8%)	0	1 (1.6%)	0	0	0	0	0	0	1 (0.2%)	2 (0.3%)
Week 33 to 40	1 (0.8%)	0	0	0	0	0	0	0	0	0	1 (0.1%)
Week 41 to 48	0	0	0	0	0	0	0	0	0	0	0
Week 49 or later	0	0	0	0	0	0	0	0	1 (1.6%)	1 (0.2%)	1 (0.1%)

System Organ Class Preferred Term Time Period	Imeglimin N = 134	Imeglimin + SU N = 127	Imeglimin + GLIN N = 64	Imeglimin + BIG N = 64	Imeglimin + AGI N = 64	Imeglimin + TZD N = 65	Imeglimin + DPP4-I N = 63	Imeglimin + GLP1-RA N = 70	Imeglimin + SGLT2-I N = 63	Combination Total N = 580	Imeglimin Total N = 714
Spinal osteoarthritis (変形性脊椎症)											
Week 1 to 4	0	0	0	0	1 (1.6%)	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 5 to 8	1 (0.7%)	0	0	0	0	0	0	0	0	0	1 (0.1%)
Week 9 to 16	0	0	0	0	0	0	1 (1.6%)	0	0	1 (0.2%)	1 (0.1%)
Week 17 to 24	0	0	0	0	0	0	0	0	0	0	0
Week 25 to 32	0	0	0	0	0	0	1 (1.6%)	0	0	1 (0.2%)	1 (0.1%)
Week 33 to 40	0	0	0	0	0	0	1 (1.6%)	1 (1.4%)	1 (1.6%)	3 (0.5%)	3 (0.4%)
Week 41 to 48	0	0	0	0	0	0	0	0	0	0	0
Week 49 or later	0	0	0	0	0	0	1 (1.7%)	0	0	1 (0.2%)	1 (0.1%)
Intervertebral disc protrusion (椎間板突出)											
Week 1 to 4	0	0	0	0	0	0	0	0	0	0	0
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	0	0	0	0	0	0	2 (3.2%)	0	0	2 (0.3%)	2 (0.3%)
Week 17 to 24	0	0	0	0	0	0	1 (1.6%)	1 (1.4%)	0	2 (0.3%)	2 (0.3%)
Week 25 to 32	0	0	0	0	0	0	1 (1.6%)	0	0	1 (0.2%)	1 (0.1%)
Week 33 to 40	0	0	0	0	1 (1.6%)	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 41 to 48	0	0	0	0	0	0	0	0	0	0	0
Week 49 or later	0	0	1 (1.7%)	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Osteoarthritis (変形性関節症)											
Week 1 to 4	1 (0.7%)	0	0	0	0	0	0	0	0	0	1 (0.1%)
Week 5 to 8	0	0	1 (1.6%)	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 9 to 16	1 (0.8%)	0	0	1 (1.6%)	0	0	0	0	0	1 (0.2%)	2 (0.3%)
Week 17 to 24	0	0	0	0	0	0	1 (1.6%)	0	0	1 (0.2%)	1 (0.1%)
Week 25 to 32	0	0	0	0	0	0	0	0	0	0	0
Week 33 to 40	0	0	0	0	0	0	0	0	0	0	0
Week 41 to 48	0	0	0	0	0	0	0	0	0	0	0

System Organ Class Preferred Term Time Period	Imeglimin N = 134	Imeglimin + SU N = 127	Imeglimin + GLIN N = 64	Imeglimin + BIG N = 64	Imeglimin + AGI N = 64	Imeglimin + TZD N = 65	Imeglimin + DPP4-I N = 63	Imeglimin + GLP1-RA N = 70	Imeglimin + SGLT2-I N = 63	Combination Total N = 580	Imeglimin Total N = 714
Week 49 or later	0	0	0	0	0	0	1 (1.7%)	0	0	1 (0.2%)	1 (0.1%)
Lumbar spinal stenosis (腰部脊柱管狭窄症)											
Week 1 to 4	0	0	0	0	0	0	0	0	0	0	0
Week 5 to 8	1 (0.7%)	0	0	0	0	0	0	0	0	0	1 (0.1%)
Week 9 to 16	0	0	0	0	0	0	0	0	0	0	0
Week 17 to 24	0	0	0	0	0	0	0	0	0	0	0
Week 25 to 32	0	0	0	0	0	0	1 (1.6%)	1 (1.4%)	0	2 (0.4%)	2 (0.3%)
Week 33 to 40	0	0	0	0	0	0	0	1 (1.4%)	0	1 (0.2%)	1 (0.1%)
Week 41 to 48	0	0	0	0	0	0	0	0	0	0	0
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Muscle spasms (筋痙縮)											
Week 1 to 4	0	0	0	0	0	0	0	0	0	0	0
Week 5 to 8	0	0	1 (1.6%)	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 9 to 16	0	0	1 (1.6%)	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 17 to 24	0	0	0	0	0	0	0	0	0	0	0
Week 25 to 32	0	1 (0.8%)	0	0	0	0	1 (1.6%)	0	0	2 (0.4%)	2 (0.3%)
Week 33 to 40	0	0	0	0	0	0	0	0	0	0	0
Week 41 to 48	0	0	0	0	0	0	0	0	0	0	0
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Musculoskeletal stiffness (筋骨格硬直)											
Week 1 to 4	0	0	0	0	0	0	0	0	0	0	0
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	0	1 (0.8%)	0	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 17 to 24	0	0	0	0	0	0	0	0	0	0	0
Week 25 to 32	0	1 (0.8%)	0	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 33 to 40	0	0	1 (1.6%)	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)

System Organ Class Preferred Term Time Period	Imeglimin N = 134	Imeglimin + SU N = 127	Imeglimin + GLIN N = 64	Imeglimin + BIG N = 64	Imeglimin + AGI N = 64	Imeglimin + TZD N = 65	Imeglimin + DPP4-I N = 63	Imeglimin + GLP1-RA N = 70	Imeglimin + SGLT2-I N = 63	Combination Total N = 580	Imeglimin Total N = 714
Week 41 to 48	0	0	1 (1.7%)	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Trigger finger (弾発指)											
Week 1 to 4	0	0	0	0	0	0	1 (1.6%)	0	0	1 (0.2%)	1 (0.1%)
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	0	0	0	0	0	0	0	0	0	0	0
Week 17 to 24	0	0	0	0	0	0	0	0	0	0	0
Week 25 to 32	0	0	0	0	0	0	0	1 (1.4%)	0	1 (0.2%)	1 (0.1%)
Week 33 to 40	0	0	0	0	0	0	0	1 (1.4%)	0	1 (0.2%)	1 (0.1%)
Week 41 to 48	0	0	0	0	0	0	1 (1.7%)	0	0	1 (0.2%)	1 (0.1%)
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Skin and subcutaneous tissue disorders (皮膚および皮下組織障害)											
Eczema (湿疹)											
Week 1 to 4	0	0	1 (1.6%)	0	0	0	1 (1.6%)	0	0	2 (0.3%)	2 (0.3%)
Week 5 to 8	1 (0.7%)	0	0	0	0	0	1 (1.6%)	1 (1.4%)	0	2 (0.3%)	3 (0.4%)
Week 9 to 16	1 (0.8%)	1 (0.8%)	0	0	0	0	1 (1.6%)	1 (1.4%)	1 (1.6%)	4 (0.7%)	5 (0.7%)
Week 17 to 24	0	1 (0.8%)	2 (3.2%)	0	0	0	1 (1.6%)	0	0	4 (0.7%)	4 (0.6%)
Week 25 to 32	0	0	0	0	0	1 (1.5%)	1 (1.6%)	2 (2.9%)	0	4 (0.7%)	4 (0.6%)
Week 33 to 40	0	1 (0.8%)	0	0	0	0	0	0	1 (1.6%)	2 (0.4%)	2 (0.3%)
Week 41 to 48	0	1 (0.8%)	0	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Acne (ざ瘡)											
Week 1 to 4	0	0	0	1 (1.6%)	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	0	1 (0.8%)	0	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)

System Organ Class Preferred Term Time Period	Imeglimin N = 134	Imeglimin + SU N = 127	Imeglimin + GLIN N = 64	Imeglimin + BIG N = 64	Imeglimin + AGI N = 64	Imeglimin + TZD N = 65	Imeglimin + DPP4-I N = 63	Imeglimin + GLP1-RA N = 70	Imeglimin + SGLT2-I N = 63	Combination Total N = 580	Imeglimin Total N = 714
Week 17 to 24	0	0	1 (1.6%)	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 25 to 32	0	0	0	0	0	0	0	0	0	0	0
Week 33 to 40	0	0	0	0	0	0	0	0	0	0	0
Week 41 to 48	0	0	1 (1.7%)	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Hyperkeratosis (過角化)											
Week 1 to 4	0	0	0	0	0	0	0	0	0	0	0
Week 5 to 8	0	1 (0.8%)	0	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 9 to 16	0	0	0	0	0	0	0	0	0	0	0
Week 17 to 24	0	0	0	0	0	0	0	0	1 (1.6%)	1 (0.2%)	1 (0.1%)
Week 25 to 32	0	0	0	0	0	0	0	0	0	0	0
Week 33 to 40	0	0	0	0	0	0	0	0	1 (1.6%)	1 (0.2%)	1 (0.1%)
Week 41 to 48	0	0	0	0	0	0	0	0	0	0	0
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Injury, poisoning and procedural complications (傷害、中毒および処置合併症)											
Contusion (挫傷)											
Week 1 to 4	0	0	0	1 (1.6%)	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 5 to 8	0	0	0	0	0	0	1 (1.6%)	0	0	1 (0.2%)	1 (0.1%)
Week 9 to 16	0	0	0	0	0	0	0	0	0	0	0
Week 17 to 24	2 (1.5%)	0	0	0	0	0	0	0	0	0	2 (0.3%)
Week 25 to 32	0	1 (0.8%)	0	0	0	0	1 (1.6%)	0	0	2 (0.4%)	2 (0.3%)
Week 33 to 40	0	1 (0.8%)	0	1 (1.7%)	0	0	0	0	0	2 (0.4%)	2 (0.3%)
Week 41 to 48	1 (0.8%)	1 (0.8%)	0	0	0	0	0	0	0	1 (0.2%)	2 (0.3%)
Week 49 or later	0	0	0	0	0	0	1 (1.7%)	0	0	1 (0.2%)	1 (0.1%)
Ligament sprain (靱帯捻挫)											

System Organ Class Preferred Term Time Period	Imeglimin N = 134	Imeglimin + SU N = 127	Imeglimin + GLIN N = 64	Imeglimin + BIG N = 64	Imeglimin + AGI N = 64	Imeglimin + TZD N = 65	Imeglimin + DPP4-I N = 63	Imeglimin + GLP1-RA N = 70	Imeglimin + SGLT2-I N = 63	Combination Total N = 580	Imeglimin Total N = 714
Week 1 to 4	0	0	1 (1.6%)	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	0	0	1 (1.6%)	0	0	1 (1.5%)	0	1 (1.4%)	0	3 (0.5%)	3 (0.4%)
Week 17 to 24	0	0	0	0	0	0	0	0	0	0	0
Week 25 to 32	1 (0.8%)	0	0	0	0	0	0	0	0	0	1 (0.1%)
Week 33 to 40	0	1 (0.8%)	0	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 41 to 48	0	0	0	0	0	0	0	0	0	0	0
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Thermal burn (熱傷)											
Week 1 to 4	0	0	0	0	0	0	0	0	0	0	0
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	0	0	0	2 (3.1%)	0	0	0	0	0	2 (0.3%)	2 (0.3%)
Week 17 to 24	0	0	0	0	0	0	1 (1.6%)	0	0	1 (0.2%)	1 (0.1%)
Week 25 to 32	0	0	0	0	0	0	0	1 (1.4%)	0	1 (0.2%)	1 (0.1%)
Week 33 to 40	1 (0.8%)	0	0	0	0	0	0	0	0	0	1 (0.1%)
Week 41 to 48	0	0	0	0	0	0	0	0	0	0	0
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Radius fracture (橈骨骨折)											
Week 1 to 4	0	0	0	0	0	0	0	0	0	0	0
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	0	0	0	0	0	0	1 (1.6%)	0	0	1 (0.2%)	1 (0.1%)
Week 17 to 24	0	0	0	0	0	0	0	0	0	0	0
Week 25 to 32	0	0	0	0	0	0	0	0	0	0	0
Week 33 to 40	0	0	0	0	0	0	0	0	0	0	0
Week 41 to 48	0	0	0	0	0	0	0	0	0	0	0
Week 49 or later	1 (0.8%)	0	0	0	0	0	1 (1.7%)	0	0	1 (0.2%)	2 (0.3%)
Tendon rupture (腱断裂)											
Week 1 to 4	0	0	0	0	0	0	0	0	0	0	0
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0

System Organ Class Preferred Term Time Period	Imeglimin N = 134	Imeglimin + SU N = 127	Imeglimin + GLIN N = 64	Imeglimin + BIG N = 64	Imeglimin + AGI N = 64	Imeglimin + TZD N = 65	Imeglimin + DPP4-I N = 63	Imeglimin + GLP1-RA N = 70	Imeglimin + SGLT2-I N = 63	Combination Total N = 580	Imeglimin Total N = 714
Week 9 to 16	0	0	0	0	0	0	0	0	0	0	0
Week 17 to 24	0	0	0	0	0	0	0	0	0	0	0
Week 25 to 32	0	0	1 (1.6%)	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 33 to 40	0	0	1 (1.6%)	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 41 to 48	0	0	0	0	0	0	0	0	0	0	0
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Nervous system disorders (神経系障害)											
Headache (頭痛)											
Week 1 to 4	0	0	0	0	0	0	0	0	0	0	0
Week 5 to 8	0	0	0	0	0	1 (1.5%)	0	0	0	1 (0.2%)	1 (0.1%)
Week 9 to 16	1 (0.8%)	0	0	0	0	0	0	0	0	0	1 (0.1%)
Week 17 to 24	1 (0.8%)	0	1 (1.6%)	0	1 (1.6%)	0	0	0	0	2 (0.3%)	3 (0.4%)
Week 25 to 32	0	0	0	0	0	0	0	0	1 (1.6%)	1 (0.2%)	1 (0.1%)
Week 33 to 40	0	1 (0.8%)	0	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 41 to 48	0	0	0	0	0	0	0	0	0	0	0
Week 49 or later	0	0	0	0	0	1 (1.5%)	0	0	0	1 (0.2%)	1 (0.1%)
Diabetic neuropathy (糖尿病性ニューロパチー)											
Week 1 to 4	0	0	0	0	0	0	0	1 (1.4%)	0	1 (0.2%)	1 (0.1%)
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	0	0	0	0	0	0	1 (1.6%)	0	0	1 (0.2%)	1 (0.1%)
Week 17 to 24	1 (0.8%)	0	0	0	0	0	0	1 (1.4%)	1 (1.6%)	2 (0.3%)	3 (0.4%)
Week 25 to 32	0	0	0	0	0	0	1 (1.6%)	0	0	1 (0.2%)	1 (0.1%)
Week 33 to 40	0	0	0	0	0	0	0	0	0	0	0
Week 41 to 48	0	0	0	0	0	0	0	0	0	0	0
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0

System Organ Class Preferred Term Time Period	Imeglimin N = 134	Imeglimin + SU N = 127	Imeglimin + GLIN N = 64	Imeglimin + BIG N = 64	Imeglimin + AGI N = 64	Imeglimin + TZD N = 65	Imeglimin + DPP4-I N = 63	Imeglimin + GLP1-RA N = 70	Imeglimin + SGLT2-I N = 63	Combination Total N = 580	Imeglimin Total N = 714
Carotid arteriosclerosis (頚動脈硬化症)											
Week 1 to 4	0	0	0	0	0	0	0	0	0	0	0
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	0	0	0	0	0	0	0	0	0	0	0
Week 17 to 24	0	0	0	0	0	0	0	0	0	0	0
Week 25 to 32	0	0	0	0	0	0	0	0	0	0	0
Week 33 to 40	0	0	0	0	0	0	0	0	0	0	0
Week 41 to 48	0	0	0	1 (1.7%)	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 49 or later	0	0	1 (1.7%)	0	0	2 (3.1%)	0	0	0	3 (0.5%)	3 (0.4%)
Cervicobrachial syndrome (頚腕症候群)											
Week 1 to 4	0	0	0	0	0	0	0	0	0	0	0
Week 5 to 8	0	0	0	0	1 (1.6%)	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 9 to 16	1 (0.8%)	0	0	0	0	0	0	0	0	0	1 (0.1%)
Week 17 to 24	0	0	0	0	1 (1.6%)	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 25 to 32	0	0	0	0	0	0	0	0	0	0	0
Week 33 to 40	0	0	0	0	0	0	0	0	0	0	0
Week 41 to 48	0	0	0	0	0	0	0	0	0	0	0
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Intercostal neuralgia (肋間神経痛)											
Week 1 to 4	0	0	0	0	0	0	0	0	0	0	0
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	0	0	2 (3.2%)	0	0	0	0	0	0	2 (0.3%)	2 (0.3%)
Week 17 to 24	0	0	0	0	0	0	0	0	0	0	0
Week 25 to 32	0	0	0	0	0	0	0	0	0	0	0
Week 33 to 40	0	0	0	0	0	0	0	0	0	0	0

System Organ Class Preferred Term Time Period	Imeglimin N = 134	Imeglimin + SU N = 127	Imeglimin + GLIN N = 64	Imeglimin + BIG N = 64	Imeglimin + AGI N = 64	Imeglimin + TZD N = 65	Imeglimin + DPP4-I N = 63	Imeglimin + GLP1-RA N = 70	Imeglimin + SGLT2-I N = 63	Combination Total N = 580	Imeglimin Total N = 714
Week 41 to 48	0	0	1 (1.7%)	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Respiratory, thoracic and mediastinal disorders (呼吸器、胸郭および縦隔障害)											
Upper respiratory tract inflammation (上気道の炎症)											
Week 1 to 4	0	0	0	0	0	0	0	0	1 (1.6%)	1 (0.2%)	1 (0.1%)
Week 5 to 8	0	0	1 (1.6%)	0	0	0	1 (1.6%)	0	0	2 (0.3%)	2 (0.3%)
Week 9 to 16	1 (0.8%)	0	0	0	0	0	0	0	1 (1.6%)	1 (0.2%)	2 (0.3%)
Week 17 to 24	0	0	0	0	1 (1.6%)	0	0	0	1 (1.6%)	2 (0.3%)	2 (0.3%)
Week 25 to 32	0	1 (0.8%)	1 (1.6%)	0	0	0	0	0	0	2 (0.4%)	2 (0.3%)
Week 33 to 40	0	0	0	0	0	1 (1.5%)	0	0	0	1 (0.2%)	1 (0.1%)
Week 41 to 48	0	0	0	0	0	1 (1.5%)	0	0	0	1 (0.2%)	1 (0.1%)
Week 49 or later	0	0	0	0	0	0	1 (1.7%)	0	0	1 (0.2%)	1 (0.1%)
Cough (咳嗽)											
Week 1 to 4	0	0	0	0	0	0	0	0	0	0	0
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	1 (0.8%)	2 (1.6%)	0	0	0	0	0	0	0	2 (0.3%)	3 (0.4%)
Week 17 to 24	1 (0.8%)	0	1 (1.6%)	0	0	0	0	1 (1.4%)	0	2 (0.3%)	3 (0.4%)
Week 25 to 32	1 (0.8%)	0	0	0	0	1 (1.5%)	0	0	0	1 (0.2%)	2 (0.3%)
Week 33 to 40	0	0	0	0	0	0	0	0	0	0	0
Week 41 to 48	0	0	0	0	0	0	0	0	0	0	0
Week 49 or later	0	0	0	1 (1.7%)	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Vascular disorders (血管障害)											
Hypertension (高血圧)											

System Organ Class Preferred Term Time Period	Imeglimin N = 134	Imeglimin + SU N = 127	Imeglimin + GLIN N = 64	Imeglimin + BIG N = 64	Imeglimin + AGI N = 64	Imeglimin + TZD N = 65	Imeglimin + DPP4-I N = 63	Imeglimin + GLP1-RA N = 70	Imeglimin + SGLT2-I N = 63	Combination Total N = 580	Imeglimin Total N = 714
Week 1 to 4	0	1 (0.8%)	0	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 5 to 8	0	0	0	0	0	1 (1.5%)	0	1 (1.4%)	0	2 (0.3%)	2 (0.3%)
Week 9 to 16	0	0	0	0	0	0	0	0	0	0	0
Week 17 to 24	0	1 (0.8%)	1 (1.6%)	0	0	0	0	0	0	2 (0.3%)	2 (0.3%)
Week 25 to 32	0	3 (2.4%)	1 (1.6%)	0	2 (3.1%)	1 (1.5%)	0	0	0	7 (1.2%)	7 (1.0%)
Week 33 to 40	0	0	0	1 (1.7%)	0	0	0	0	1 (1.6%)	2 (0.4%)	2 (0.3%)
Week 41 to 48	0	0	0	0	0	1 (1.5%)	0	1 (1.4%)	0	2 (0.4%)	2 (0.3%)
Week 49 or later	0	2 (1.7%)	0	0	1 (1.6%)	0	1 (1.7%)	0	0	4 (0.7%)	4 (0.6%)
Renal and urinary disorders (腎および尿路障害)											
Diabetic nephropathy (糖尿病性腎症)											
Week 1 to 4	0	1 (0.8%)	0	0	2 (3.1%)	0	1 (1.6%)	0	1 (1.6%)	5 (0.9%)	5 (0.7%)
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	0	0	0	0	0	0	0	0	0	0	0
Week 17 to 24	0	0	0	0	0	0	0	0	0	0	0
Week 25 to 32	0	0	0	1 (1.6%)	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 33 to 40	0	0	0	0	0	0	0	0	0	0	0
Week 41 to 48	0	0	0	0	0	1 (1.5%)	0	0	0	1 (0.2%)	1 (0.1%)
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Nephrolithiasis (腎結石症)											
Week 1 to 4	0	0	0	0	1 (1.6%)	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 5 to 8	1 (0.7%)	0	0	0	0	0	0	0	0	0	1 (0.1%)
Week 9 to 16	0	0	0	0	1 (1.6%)	0	0	1 (1.4%)	0	2 (0.3%)	2 (0.3%)
Week 17 to 24	0	0	0	0	0	0	1 (1.6%)	0	0	1 (0.2%)	1 (0.1%)
Week 25 to 32	0	0	0	0	0	1 (1.5%)	0	0	0	1 (0.2%)	1 (0.1%)
Week 33 to 40	0	0	0	0	0	0	0	0	0	0	0

System Organ Class Preferred Term Time Period	Imeglimin N = 134	Imeglimin + SU N = 127	Imeglimin + GLIN N = 64	Imeglimin + BIG N = 64	Imeglimin + AGI N = 64	Imeglimin + TZD N = 65	Imeglimin + DPP4-I N = 63	Imeglimin + GLP1-RA N = 70	Imeglimin + SGLT2-I N = 63	Combination Total N = 580	Imeglimin Total N = 714
Week 41 to 48	0	0	0	0	0	1 (1.5%)	0	0	0	1 (0.2%)	1 (0.1%)
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Pollakiuria (頻尿)											
Week 1 to 4	0	0	0	0	0	0	0	0	0	0	0
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	0	0	0	0	0	0	0	0	0	0	0
Week 17 to 24	0	0	0	0	0	0	0	0	1 (1.6%)	1 (0.2%)	1 (0.1%)
Week 25 to 32	0	0	0	0	0	0	0	1 (1.4%)	0	1 (0.2%)	1 (0.1%)
Week 33 to 40	0	0	0	0	0	0	0	1 (1.4%)	0	1 (0.2%)	1 (0.1%)
Week 41 to 48	0	0	0	0	0	0	0	0	0	0	0
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Eye disorders (眼障害)											
Diabetic retinopathy (糖尿病網膜症)											
Week 1 to 4	0	0	0	0	0	0	0	1 (1.4%)	0	1 (0.2%)	1 (0.1%)
Week 5 to 8	0	0	1 (1.6%)	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 9 to 16	0	0	0	0	0	1 (1.5%)	0	0	0	1 (0.2%)	1 (0.1%)
Week 17 to 24	0	0	0	0	0	1 (1.5%)	1 (1.6%)	0	0	2 (0.3%)	2 (0.3%)
Week 25 to 32	1 (0.8%)	1 (0.8%)	0	0	0	0	1 (1.6%)	0	0	2 (0.4%)	3 (0.4%)
Week 33 to 40	0	0	0	0	0	0	1 (1.6%)	0	0	1 (0.2%)	1 (0.1%)
Week 41 to 48	1 (0.8%)	0	0	0	0	0	0	0	0	0	1 (0.1%)
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Asthenopia (眼精疲労)											
Week 1 to 4	0	0	0	0	0	0	0	1 (1.4%)	0	1 (0.2%)	1 (0.1%)
Week 5 to 8	0	0	1 (1.6%)	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 9 to 16	0	0	0	0	0	0	0	0	0	0	0
Week 17 to 24	0	1 (0.8%)	0	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)

System Organ Class Preferred Term Time Period	Imeglimin N = 134	Imeglimin + SU N = 127	Imeglimin + GLIN N = 64	Imeglimin + BIG N = 64	Imeglimin + AGI N = 64	Imeglimin + TZD N = 65	Imeglimin + DPP4-I N = 63	Imeglimin + GLP1-RA N = 70	Imeglimin + SGLT2-I N = 63	Combination Total N = 580	Imeglimin Total N = 714
Week 25 to 32	0	0	0	0	0	0	0	0	0	0	0
Week 33 to 40	0	0	0	0	0	0	0	0	0	0	0
Week 41 to 48	0	0	1 (1.7%)	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Psychiatric disorders (精神障害)											
Insomnia (不眠症)											
Week 1 to 4	0	1 (0.8%)	0	1 (1.6%)	0	0	1 (1.6%)	0	0	3 (0.5%)	3 (0.4%)
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	0	0	0	1 (1.6%)	0	0	1 (1.6%)	0	0	2 (0.3%)	2 (0.3%)
Week 17 to 24	0	0	0	0	0	0	0	0	0	0	0
Week 25 to 32	2 (1.5%)	0	0	0	0	0	0	0	1 (1.6%)	1 (0.2%)	3 (0.4%)
Week 33 to 40	0	0	0	0	0	0	0	0	0	0	0
Week 41 to 48	0	0	0	0	0	0	1 (1.7%)	1 (1.4%)	0	2 (0.4%)	2 (0.3%)
Week 49 or later	0	0	0	0	0	1 (1.5%)	0	0	0	1 (0.2%)	1 (0.1%)
Hepatobiliary disorders (肝胆道系障害)											
Hepatic steatosis (脂肪肝)											
Week 1 to 4	0	0	0	0	0	0	0	0	0	0	0
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	0	0	0	0	0	0	0	2 (2.9%)	0	2 (0.3%)	2 (0.3%)
Week 17 to 24	0	1 (0.8%)	1 (1.6%)	0	0	0	0	0	0	2 (0.3%)	2 (0.3%)
Week 25 to 32	0	0	0	0	0	1 (1.5%)	0	0	0	1 (0.2%)	1 (0.1%)
Week 33 to 40	0	0	0	0	0	0	0	0	0	0	0
Week 41 to 48	0	0	0	0	0	0	0	0	0	0	0
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0

System Organ Class Preferred Term Time Period	Imeglimin N = 134	Imeglimin + SU N = 127	Imeglimin + GLIN N = 64	Imeglimin + BIG N = 64	Imeglimin + AGI N = 64	Imeglimin + TZD N = 65	Imeglimin + DPP4-I N = 63	Imeglimin + GLP1-RA N = 70	Imeglimin + SGLT2-I N = 63	Combination Total N = 580	Imeglimin Total N = 714
Alcoholic liver disease (アルコール性肝疾患)											
Week 1 to 4	0	0	0	0	0	0	0	0	0	0	0
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	0	0	0	0	0	0	0	1 (1.4%)	0	1 (0.2%)	1 (0.1%)
Week 17 to 24	0	0	0	0	0	0	0	0	0	0	0
Week 25 to 32	0	1 (0.8%)	0	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 33 to 40	0	0	0	0	0	0	0	1 (1.4%)	0	1 (0.2%)	1 (0.1%)
Week 41 to 48	0	0	0	0	0	0	0	0	0	0	0
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Cholelithiasis (胆石症)											
Week 1 to 4	0	0	0	0	0	0	0	0	0	0	0
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	0	0	0	0	0	0	0	1 (1.4%)	0	1 (0.2%)	1 (0.1%)
Week 17 to 24	0	0	0	0	0	0	0	0	0	0	0
Week 25 to 32	0	0	0	0	0	0	0	1 (1.4%)	0	1 (0.2%)	1 (0.1%)
Week 33 to 40	0	0	0	0	0	0	0	0	0	0	0
Week 41 to 48	0	0	0	0	1 (1.6%)	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Gallbladder polyp (胆嚢ポリープ)											
Week 1 to 4	0	0	0	0	0	0	0	0	0	0	0
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	0	0	0	0	0	0	0	2 (2.9%)	0	2 (0.3%)	2 (0.3%)
Week 17 to 24	0	0	0	0	0	0	0	0	0	0	0
Week 25 to 32	0	0	0	0	0	0	0	0	0	0	0
Week 33 to 40	0	0	0	0	0	0	0	0	0	0	0
Week 41 to 48	0	0	0	0	0	0	0	0	0	0	0

System Organ Class Preferred Term Time Period	Imeglimin N = 134	Imeglimin + SU N = 127	Imeglimin + GLIN N = 64	Imeglimin + BIG N = 64	Imeglimin + AGI N = 64	Imeglimin + TZD N = 65	Imeglimin + DPP4-I N = 63	Imeglimin + GLP1-RA N = 70	Imeglimin + SGLT2-I N = 63	Combination Total N = 580	Imeglimin Total N = 714
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Investigations (臨床検査)											
Lipase increased (リパーゼ増加)											
Week 1 to 4	0	0	0	0	0	0	0	0	0	0	0
Week 5 to 8	0	1 (0.8%)	0	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 9 to 16	0	1 (0.8%)	0	0	0	1 (1.5%)	2 (3.2%)	0	0	4 (0.7%)	4 (0.6%)
Week 17 to 24	1 (0.8%)	0	0	0	0	0	0	0	0	0	1 (0.1%)
Week 25 to 32	0	0	0	0	1 (1.6%)	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 33 to 40	0	0	0	0	0	0	0	0	0	0	0
Week 41 to 48	0	0	0	0	0	0	1 (1.7%)	0	0	1 (0.2%)	1 (0.1%)
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Surgical and medical procedures (外科および内科処置)											
Cataract operation (白内障手術)											
Week 1 to 4	0	0	0	0	0	0	0	0	0	0	0
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	0	0	1 (1.6%)	2 (3.1%)	1 (1.6%)	0	0	0	0	4 (0.7%)	4 (0.6%)
Week 17 to 24	1 (0.8%)	1 (0.8%)	0	0	0	0	0	0	0	1 (0.2%)	2 (0.3%)
Week 25 to 32	0	2 (1.6%)	0	0	0	0	0	0	0	2 (0.4%)	2 (0.3%)
Week 33 to 40	0	0	0	0	0	0	0	0	0	0	0
Week 41 to 48	0	0	0	0	0	0	0	0	0	0	0
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Cardiac disorders (心臓障害)											

System Organ Class Preferred Term Time Period	Imeglimin N = 134	Imeglimin + SU N = 127	Imeglimin + GLIN N = 64	Imeglimin + BIG N = 64	Imeglimin + AGI N = 64	Imeglimin + TZD N = 65	Imeglimin + DPP4-I N = 63	Imeglimin + GLP1-RA N = 70	Imeglimin + SGLT2-I N = 63	Combination Total N = 580	Imeglimin Total N = 714
Coronary artery stenosis (冠動脈狭窄)											
Week 1 to 4	0	0	0	0	0	0	0	0	0	0	0
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	0	0	0	0	0	0	0	0	0	0	0
Week 17 to 24	0	0	0	0	0	0	0	0	0	0	0
Week 25 to 32	0	0	0	0	0	0	0	0	0	0	0
Week 33 to 40	0	0	0	0	0	0	0	1 (1.4%)	0	1 (0.2%)	1 (0.1%)
Week 41 to 48	0	0	0	0	0	0	0	1 (1.4%)	0	1 (0.2%)	1 (0.1%)
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Palpitations (動悸)											
Week 1 to 4	0	0	0	0	0	0	0	0	0	0	0
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	0	0	0	1 (1.6%)	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 17 to 24	0	0	0	1 (1.6%)	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 25 to 32	0	0	0	0	0	0	0	0	0	0	0
Week 33 to 40	0	0	0	0	0	0	0	0	0	0	0
Week 41 to 48	0	0	0	0	0	0	0	0	0	0	0
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Sinus bradycardia (洞性徐脈)											
Week 1 to 4	0	0	0	0	0	0	0	0	0	0	0
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	0	0	0	0	0	0	0	0	0	0	0
Week 17 to 24	0	0	0	0	0	1 (1.5%)	0	0	0	1 (0.2%)	1 (0.1%)
Week 25 to 32	0	0	0	0	0	0	0	0	0	0	0
Week 33 to 40	0	0	0	0	0	0	0	0	0	0	0
Week 41 to 48	0	0	0	0	0	0	0	0	0	0	0
Week 49 or later	0	0	0	0	0	1 (1.5%)	0	0	0	1 (0.2%)	1 (0.1%)

System Organ Class Preferred Term Time Period	Imeglimin N = 134	Imeglimin + SU N = 127	Imeglimin + GLIN N = 64	Imeglimin + BIG N = 64	Imeglimin + AGI N = 64	Imeglimin + TZD N = 65	Imeglimin + DPP4-I N = 63	Imeglimin + GLP1-RA N = 70	Imeglimin + SGLT2-I N = 63	Combination Total N = 580	Imeglimin Total N = 714
General disorders and administration site conditions (一般・全身障害および投与部位の状態)											
Fatigue (疲労)											
Week 1 to 4	0	0	0	0	0	0	0	0	0	0	0
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	1 (0.8%)	0	0	0	0	0	0	0	0	0	1 (0.1%)
Week 17 to 24	0	0	0	0	0	0	1 (1.6%)	0	0	1 (0.2%)	1 (0.1%)
Week 25 to 32	0	0	1 (1.6%)	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 33 to 40	0	0	0	0	0	0	0	0	1 (1.6%)	1 (0.2%)	1 (0.1%)
Week 41 to 48	0	0	0	0	0	0	1 (1.7%)	0	0	1 (0.2%)	1 (0.1%)
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Ear and labyrinth disorders (耳および迷路障害)											
Vertigo (回転性めまい)											
Week 1 to 4	0	0	0	0	0	0	0	0	0	0	0
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	1 (0.8%)	0	0	2 (3.1%)	0	0	0	0	0	2 (0.3%)	3 (0.4%)
Week 17 to 24	0	0	0	0	0	0	0	0	0	0	0
Week 25 to 32	0	0	0	0	0	0	0	0	0	0	0
Week 33 to 40	0	0	0	0	0	0	0	0	0	0	0
Week 41 to 48	0	0	0	0	0	0	0	1 (1.4%)	0	1 (0.2%)	1 (0.1%)
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0

System Organ Class Preferred Term Time Period	Imeglimin N = 134	Imeglimin + SU N = 127	Imeglimin + GLIN N = 64	Imeglimin + BIG N = 64	Imeglimin + AGI N = 64	Imeglimin + TZD N = 65	Imeglimin + DPP4-I N = 63	Imeglimin + GLP1-RA N = 70	Imeglimin + SGLT2-I N = 63	Combination Total N = 580	Imeglimin Total N = 714
Reproductive system and breast disorders (生殖系および乳房障害)											
Benign prostatic hyperplasia (良性前立腺肥大症)											
Week 1 to 4	0	0	0	0	0	0	0	0	0	0	0
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	1 (0.8%)	0	0	0	0	0	0	0	0	0	1 (0.1%)
Week 17 to 24	0	0	1 (1.6%)	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 25 to 32	0	0	0	0	0	0	0	0	0	0	0
Week 33 to 40	0	0	0	0	0	0	0	0	0	0	0
Week 41 to 48	0	0	0	0	0	0	0	0	0	0	0
Week 49 or later	0	0	1 (1.7%)	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Immune system disorders (免疫系障害)											
Allergy to arthropod sting (節足動物刺傷アレルギー)											
Week 1 to 4	0	0	0	0	0	0	0	0	0	0	0
Week 5 to 8	0	0	0	0	0	0	0	1 (1.4%)	0	1 (0.2%)	1 (0.1%)
Week 9 to 16	0	0	0	0	0	0	0	0	0	0	0
Week 17 to 24	0	0	0	0	0	0	0	0	0	0	0
Week 25 to 32	0	0	0	0	0	0	0	0	0	0	0
Week 33 to 40	0	0	0	0	0	0	0	1 (1.4%)	0	1 (0.2%)	1 (0.1%)
Week 41 to 48	0	0	0	0	0	0	0	0	0	0	0

System Organ Class Preferred Term Time Period	Imeglimin N = 134	Imeglimin + SU N = 127	Imeglimin + GLIN N = 64	Imeglimin + BIG N = 64	Imeglimin + AGI N = 64	Imeglimin + TZD N = 65	Imeglimin + DPP4-I N = 63	Imeglimin + GLP1-RA N = 70	Imeglimin + SGLT2-I N = 63	Combination Total N = 580	Imeglimin Total N = 714
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0

- Abbreviations: AE, Adverse event; TEAE, Treatment Emergent AE; SU, Sulphonylurea; GLIN, Glinide; BIG, Biguanide; AGI, Alpha glucosidase inhibitor; TZD, Thiazolidinedione; DPP4-I, Dipeptidyl peptidase-4 inhibitor; GLP1-RA, Glucagon-like peptide 1 receptor agonist; SGLT2-I, Sodium glucose cotransporter 2 inhibitor
- "Imeglimin" in this table means "Imeglimin 1000 mg twice daily".
- "Combination Total" is the sum of the subjects excluding monotherapy "Imeglimin".
- "Imeglimin Total" is the sum of all subjects in Imeglimin treatment groups.
- All adverse events were coded using MedDRA dictionary version 20.1.
- Within each subject, multiple reports of adverse events mapped to a common System Organ Class and Preferred Term are counted only once.
- Number of patients in each period is defined as that of patients whose study duration was equal to or greater than the initial day of the corresponding time period.
- Percentages are based on "Number of patients in each period".
- Time Period: Week 1 to 4 = Day 1 to 28, Week 5 to 8 = Day 29 to 56, Week 9 to 16 = Day 57 to 112, Week 17 to 24 = Day 113 to 168, Week 25 to 32 = Day 169 to 224, Week 33 to 40 = Day 225 to 280, Week 41 to 48 = Day 281 to 336, Week 49 or later = Day 337 or later.

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Table S-073 Summary of Treatment Emergent Adverse Events (Incidence >= 2%) by Timing of Every Onset, System Organ Class and Preferred Term in 52-Week Long-term Period with Monotherapy and Combination Therapy (PXL008-019; Long-term Safety Population)

System Organ Class Preferred Term Time Period	Imeglimin N = 134	Imeglimin + SU N = 127	Imeglimin + GLIN N = 64	Imeglimin + BIG N = 64	Imeglimin + AGI N = 64	Imeglimin + TZD N = 65	Imeglimin + DPP4-I N = 63	Imeglimin + GLP1-RA N = 70	Imeglimin + SGLT2-I N = 63	Combination Total N = 580	Imeglimin Total N = 714
Number of patients in each period											
Week 1 to 4	134	127	64	64	64	65	63	70	63	580	714
Week 5 to 8	134	127	63	64	64	65	63	70	63	579	713
Week 9 to 16	133	126	63	64	64	65	62	69	63	576	709
Week 17 to 24	131	123	63	64	64	65	62	69	63	573	704
Week 25 to 32	130	123	63	63	64	65	61	69	63	571	701
Week 33 to 40	128	123	61	60	63	65	61	69	63	565	693
Week 41 to 48	128	119	60	60	62	65	60	69	63	558	686
Week 49 or later	127	116	60	58	62	65	60	67	62	550	677
Any TEAE											
Week 1 to 4	18 (13.4%)	25 (19.7%)	14 (21.9%)	20 (31.3%)	5 (7.8%)	15 (23.1%)	16 (25.4%)	16 (22.9%)	13 (20.6%)	124 (21.4%)	142 (19.9%)
Week 5 to 8	16 (11.9%)	24 (18.9%)	12 (19.0%)	9 (14.1%)	3 (4.7%)	12 (18.5%)	9 (14.3%)	18 (25.7%)	9 (14.3%)	96 (16.6%)	112 (15.7%)
Week 9 to 16	30 (22.6%)	36 (28.6%)	13 (20.6%)	18 (28.1%)	7 (10.9%)	14 (21.5%)	18 (29.0%)	18 (26.1%)	12 (19.0%)	136 (23.6%)	166 (23.4%)
Week 17 to 24	28 (21.4%)	37 (30.1%)	25 (39.7%)	15 (23.4%)	11 (17.2%)	7 (10.8%)	12 (19.4%)	14 (20.3%)	19 (30.2%)	140 (24.4%)	168 (23.9%)
Week 25 to 32	34 (26.2%)	44 (35.8%)	20 (31.7%)	15 (23.8%)	12 (18.8%)	18 (27.7%)	22 (36.1%)	22 (31.9%)	17 (27.0%)	170 (29.8%)	204 (29.1%)
Week 33 to 40	18 (14.1%)	35 (28.5%)	15 (24.6%)	13 (21.7%)	8 (12.7%)	17 (26.2%)	19 (31.1%)	17 (24.6%)	15 (23.8%)	139 (24.6%)	157 (22.7%)
Week 41 to 48	28 (21.9%)	29 (24.4%)	18 (30.0%)	17 (28.3%)	6 (9.7%)	14 (21.5%)	18 (30.0%)	13 (18.8%)	11 (17.5%)	126 (22.6%)	154 (22.4%)
Week 49 or later	12 (9.4%)	14 (12.1%)	9 (15.0%)	5 (8.6%)	2 (3.2%)	12 (18.5%)	12 (20.0%)	4 (6.0%)	12 (19.4%)	70 (12.7%)	82 (12.1%)
Infections and infestations (感染症および寄生虫症)											
Nasopharyngitis (上咽頭炎)											
Week 1 to 4	3 (2.2%)	4 (3.1%)	4 (6.3%)	0	0	4 (6.2%)	2 (3.2%)	4 (5.7%)	0	18 (3.1%)	21 (2.9%)
Week 5 to 8	4 (3.0%)	1 (0.8%)	2 (3.2%)	2 (3.1%)	0	1 (1.5%)	0	5 (7.1%)	2 (3.2%)	13 (2.2%)	17 (2.4%)
Week 9 to 16	6 (4.5%)	8 (6.3%)	4 (6.3%)	0	1 (1.6%)	3 (4.6%)	4 (6.5%)	3 (4.3%)	3 (4.8%)	26 (4.5%)	32 (4.5%)

System Organ Class Preferred Term Time Period	Imeglimin N = 134	Imeglimin + SU N = 127	Imeglimin + GLIN N = 64	Imeglimin + BIG N = 64	Imeglimin + AGI N = 64	Imeglimin + TZD N = 65	Imeglimin + DPP4-I N = 63	Imeglimin + GLP1-RA N = 70	Imeglimin + SGLT2-I N = 63	Combination Total N = 580	Imeglimin Total N = 714
Week 17 to 24	2 (1.5%)	7 (5.7%)	7 (11.1%)	4 (6.3%)	0	2 (3.1%)	0	1 (1.4%)	5 (7.9%)	26 (4.5%)	28 (4.0%)
Week 25 to 32	14 (10.8%)	11 (8.9%)	6 (9.5%)	3 (4.8%)	0	6 (9.2%)	6 (9.8%)	9 (13.0%)	6 (9.5%)	47 (8.2%)	61 (8.7%)
Week 33 to 40	8 (6.3%)	14 (11.4%)	6 (9.8%)	5 (8.3%)	3 (4.8%)	4 (6.2%)	5 (8.2%)	2 (2.9%)	5 (7.9%)	44 (7.8%)	52 (7.5%)
Week 41 to 48	12 (9.4%)	3 (2.5%)	6 (10.0%)	7 (11.7%)	1 (1.6%)	1 (1.5%)	4 (6.7%)	4 (5.8%)	4 (6.3%)	30 (5.4%)	42 (6.1%)
Week 49 or later	3 (2.4%)	3 (2.6%)	1 (1.7%)	0	0	2 (3.1%)	4 (6.7%)	2 (3.0%)	2 (3.2%)	14 (2.5%)	17 (2.5%)
Pharyngitis (咽頭炎)											
Week 1 to 4	0	0	0	0	0	1 (1.5%)	1 (1.6%)	0	0	2 (0.3%)	2 (0.3%)
Week 5 to 8	0	2 (1.6%)	0	0	0	2 (3.1%)	0	0	0	4 (0.7%)	4 (0.6%)
Week 9 to 16	2 (1.5%)	1 (0.8%)	0	0	1 (1.6%)	0	1 (1.6%)	0	1 (1.6%)	4 (0.7%)	6 (0.8%)
Week 17 to 24	3 (2.3%)	0	2 (3.2%)	0	1 (1.6%)	1 (1.5%)	0	0	0	4 (0.7%)	7 (1.0%)
Week 25 to 32	2 (1.5%)	2 (1.6%)	0	0	0	0	0	0	2 (3.2%)	4 (0.7%)	6 (0.9%)
Week 33 to 40	0	0	0	0	0	0	1 (1.6%)	0	1 (1.6%)	2 (0.4%)	2 (0.3%)
Week 41 to 48	1 (0.8%)	1 (0.8%)	1 (1.7%)	0	0	0	1 (1.7%)	1 (1.4%)	1 (1.6%)	5 (0.9%)	6 (0.9%)
Week 49 or later	0	0	1 (1.7%)	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Influenza (インフルエンザ)											
Week 1 to 4	0	0	0	0	0	0	0	0	1 (1.6%)	1 (0.2%)	1 (0.1%)
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	0	0	0	0	0	0	0	1 (1.4%)	0	1 (0.2%)	1 (0.1%)
Week 17 to 24	0	1 (0.8%)	0	0	1 (1.6%)	0	0	0	0	2 (0.3%)	2 (0.3%)
Week 25 to 32	0	1 (0.8%)	0	0	0	2 (3.1%)	0	0	0	3 (0.5%)	3 (0.4%)
Week 33 to 40	0	4 (3.3%)	1 (1.6%)	2 (3.3%)	0	0	1 (1.6%)	0	0	8 (1.4%)	8 (1.2%)
Week 41 to 48	4 (3.1%)	3 (2.5%)	0	3 (5.0%)	0	1 (1.5%)	0	0	1 (1.6%)	8 (1.4%)	12 (1.7%)
Week 49 or later	0	0	1 (1.7%)	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Bronchitis (気管支炎)											
Week 1 to 4	0	0	0	0	0	1 (1.5%)	0	0	0	1 (0.2%)	1 (0.1%)
Week 5 to 8	0	0	0	0	0	1 (1.5%)	0	0	0	1 (0.2%)	1 (0.1%)
Week 9 to 16	0	0	1 (1.6%)	1 (1.6%)	0	0	0	0	0	2 (0.3%)	2 (0.3%)
Week 17 to 24	0	0	0	1 (1.6%)	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 25 to 32	1 (0.8%)	1 (0.8%)	1 (1.6%)	1 (1.6%)	0	1 (1.5%)	0	0	1 (1.6%)	5 (0.9%)	6 (0.9%)

System Organ Class Preferred Term Time Period	Imeglimin N = 134	Imeglimin + SU N = 127	Imeglimin + GLIN N = 64	Imeglimin + BIG N = 64	Imeglimin + AGI N = 64	Imeglimin + TZD N = 65	Imeglimin + DPP4-I N = 63	Imeglimin + GLP1-RA N = 70	Imeglimin + SGLT2-I N = 63	Combination Total N = 580	Imeglimin Total N = 714
Week 33 to 40	0	0	0	0	0	1 (1.5%)	0	0	1 (1.6%)	2 (0.4%)	2 (0.3%)
Week 41 to 48	0	0	1 (1.7%)	0	0	1 (1.5%)	0	0	0	2 (0.4%)	2 (0.3%)
Week 49 or later	0	0	1 (1.7%)	0	0	1 (1.5%)	0	0	1 (1.6%)	3 (0.5%)	3 (0.4%)
Gastroenteritis (胃腸炎)											
Week 1 to 4	1 (0.7%)	0	1 (1.6%)	0	0	0	0	0	0	1 (0.2%)	2 (0.3%)
Week 5 to 8	0	0	0	2 (3.1%)	0	0	0	0	0	2 (0.3%)	2 (0.3%)
Week 9 to 16	1 (0.8%)	0	0	1 (1.6%)	0	0	0	1 (1.4%)	0	2 (0.3%)	3 (0.4%)
Week 17 to 24	0	0	0	0	0	0	0	1 (1.4%)	0	1 (0.2%)	1 (0.1%)
Week 25 to 32	0	0	1 (1.6%)	1 (1.6%)	0	1 (1.5%)	0	0	0	3 (0.5%)	3 (0.4%)
Week 33 to 40	0	0	0	0	0	0	0	0	0	0	0
Week 41 to 48	0	0	1 (1.7%)	0	1 (1.6%)	0	1 (1.7%)	0	1 (1.6%)	4 (0.7%)	4 (0.6%)
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Periodontitis (歯周炎)											
Week 1 to 4	0	0	0	1 (1.6%)	0	1 (1.5%)	1 (1.6%)	0	0	3 (0.5%)	3 (0.4%)
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	0	0	0	0	0	1 (1.5%)	0	0	0	1 (0.2%)	1 (0.1%)
Week 17 to 24	0	1 (0.8%)	0	1 (1.6%)	0	0	0	0	0	2 (0.3%)	2 (0.3%)
Week 25 to 32	0	1 (0.8%)	1 (1.6%)	0	0	0	1 (1.6%)	1 (1.4%)	0	4 (0.7%)	4 (0.6%)
Week 33 to 40	0	1 (0.8%)	0	0	0	1 (1.5%)	0	0	0	2 (0.4%)	2 (0.3%)
Week 41 to 48	0	0	0	0	0	0	0	0	0	0	0
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Cystitis (膀胱炎)											
Week 1 to 4	1 (0.7%)	0	0	0	0	0	0	0	0	0	1 (0.1%)
Week 5 to 8	0	1 (0.8%)	0	0	0	0	0	1 (1.4%)	0	2 (0.3%)	2 (0.3%)
Week 9 to 16	0	0	0	0	0	1 (1.5%)	0	2 (2.9%)	0	3 (0.5%)	3 (0.4%)
Week 17 to 24	0	1 (0.8%)	1 (1.6%)	0	0	0	0	0	1 (1.6%)	3 (0.5%)	3 (0.4%)
Week 25 to 32	0	0	1 (1.6%)	0	0	0	1 (1.6%)	0	0	2 (0.4%)	2 (0.3%)
Week 33 to 40	0	0	0	0	0	0	1 (1.6%)	0	0	1 (0.2%)	1 (0.1%)
Week 41 to 48	0	0	0	0	0	0	0	0	0	0	0

System Organ Class Preferred Term Time Period	Imeglimin N = 134	Imeglimin + SU N = 127	Imeglimin + GLIN N = 64	Imeglimin + BIG N = 64	Imeglimin + AGI N = 64	Imeglimin + TZD N = 65	Imeglimin + DPP4-I N = 63	Imeglimin + GLP1-RA N = 70	Imeglimin + SGLT2-I N = 63	Combination Total N = 580	Imeglimin Total N = 714
Week 49 or later	0	0	0	0	0	1 (1.5%)	0	0	0	1 (0.2%)	1 (0.1%)
Herpes zoster (帯状疱疹)											
Week 1 to 4	0	0	0	0	0	0	0	0	1 (1.6%)	1 (0.2%)	1 (0.1%)
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	0	1 (0.8%)	0	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 17 to 24	1 (0.8%)	0	0	0	0	0	0	0	1 (1.6%)	1 (0.2%)	2 (0.3%)
Week 25 to 32	0	0	0	0	0	1 (1.5%)	0	0	0	1 (0.2%)	1 (0.1%)
Week 33 to 40	1 (0.8%)	0	0	0	0	0	1 (1.6%)	1 (1.4%)	0	2 (0.4%)	3 (0.4%)
Week 41 to 48	0	0	0	0	0	0	0	0	0	0	0
Week 49 or later	0	0	1 (1.7%)	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Upper respiratory tract infection (上気道感染)											
Week 1 to 4	0	1 (0.8%)	0	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 5 to 8	0	1 (0.8%)	0	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 9 to 16	1 (0.8%)	0	0	0	0	0	0	0	0	0	1 (0.1%)
Week 17 to 24	0	1 (0.8%)	0	0	0	0	0	0	1 (1.6%)	2 (0.3%)	2 (0.3%)
Week 25 to 32	0	0	0	0	0	0	1 (1.6%)	0	0	1 (0.2%)	1 (0.1%)
Week 33 to 40	0	0	0	0	0	0	1 (1.6%)	0	0	1 (0.2%)	1 (0.1%)
Week 41 to 48	1 (0.8%)	0	0	0	0	0	0	0	0	0	1 (0.1%)
Week 49 or later	0	1 (0.9%)	0	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Urinary tract infection (尿路感染)											
Week 1 to 4	0	0	0	0	0	0	0	0	0	0	0
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	0	0	0	0	0	2 (3.1%)	0	0	0	2 (0.3%)	2 (0.3%)
Week 17 to 24	0	0	0	0	0	0	0	0	0	0	0
Week 25 to 32	0	0	0	0	1 (1.6%)	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 33 to 40	0	0	0	0	1 (1.6%)	0	0	0	0	1 (0.2%)	1 (0.1%)

System Organ Class Preferred Term Time Period	Imeglimin N = 134	Imeglimin + SU N = 127	Imeglimin + GLIN N = 64	Imeglimin + BIG N = 64	Imeglimin + AGI N = 64	Imeglimin + TZD N = 65	Imeglimin + DPP4-I N = 63	Imeglimin + GLP1-RA N = 70	Imeglimin + SGLT2-I N = 63	Combination Total N = 580	Imeglimin Total N = 714
Week 41 to 48	0	0	0	0	1 (1.6%)	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Gingivitis (歯肉炎)											
Week 1 to 4	0	1 (0.8%)	0	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	0	0	0	0	0	0	0	1 (1.4%)	0	1 (0.2%)	1 (0.1%)
Week 17 to 24	0	0	0	0	0	0	0	1 (1.4%)	0	1 (0.2%)	1 (0.1%)
Week 25 to 32	0	0	0	0	0	0	0	0	0	0	0
Week 33 to 40	0	0	0	0	0	0	0	0	0	0	0
Week 41 to 48	0	0	0	0	0	0	0	1 (1.4%)	0	1 (0.2%)	1 (0.1%)
Week 49 or later	0	0	0	0	0	1 (1.5%)	0	0	0	1 (0.2%)	1 (0.1%)
Pericoronitis (歯冠周囲炎)											
Week 1 to 4	0	0	0	0	0	0	0	0	0	0	0
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	0	0	0	0	1 (1.6%)	0	0	1 (1.4%)	0	2 (0.3%)	2 (0.3%)
Week 17 to 24	0	0	0	0	0	0	0	1 (1.4%)	0	1 (0.2%)	1 (0.1%)
Week 25 to 32	0	0	0	0	0	0	0	0	1 (1.6%)	1 (0.2%)	1 (0.1%)
Week 33 to 40	0	0	0	0	0	0	0	0	0	0	0
Week 41 to 48	0	0	0	0	0	0	0	0	0	0	0
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Gastrointestinal disorders (胃腸障害)											
Nausea (悪心)											
Week 1 to 4	3 (2.2%)	0	0	7 (10.9%)	0	1 (1.5%)	4 (6.3%)	3 (4.3%)	2 (3.2%)	17 (2.9%)	20 (2.8%)
Week 5 to 8	2 (1.5%)	0	0	0	0	1 (1.5%)	0	0	1 (1.6%)	2 (0.3%)	4 (0.6%)
Week 9 to 16	0	1 (0.8%)	0	2 (3.1%)	0	0	0	0	0	3 (0.5%)	3 (0.4%)
Week 17 to 24	3 (2.3%)	0	0	2 (3.1%)	0	0	0	0	0	2 (0.3%)	5 (0.7%)

System Organ Class Preferred Term Time Period	Imeglimin N = 134	Imeglimin + SU N = 127	Imeglimin + GLIN N = 64	Imeglimin + BIG N = 64	Imeglimin + AGI N = 64	Imeglimin + TZD N = 65	Imeglimin + DPP4-I N = 63	Imeglimin + GLP1-RA N = 70	Imeglimin + SGLT2-I N = 63	Combination Total N = 580	Imeglimin Total N = 714
Week 25 to 32	0	0	0	1 (1.6%)	0	0	1 (1.6%)	0	1 (1.6%)	3 (0.5%)	3 (0.4%)
Week 33 to 40	0	0	0	0	0	0	0	0	0	0	0
Week 41 to 48	0	0	0	0	0	0	1 (1.7%)	0	0	1 (0.2%)	1 (0.1%)
Week 49 or later	1 (0.8%)	0	0	1 (1.7%)	1 (1.6%)	0	0	0	0	2 (0.4%)	3 (0.4%)
Diarrhoea (下痢)											
Week 1 to 4	2 (1.5%)	1 (0.8%)	3 (4.7%)	7 (10.9%)	0	2 (3.1%)	1 (1.6%)	1 (1.4%)	1 (1.6%)	16 (2.8%)	18 (2.5%)
Week 5 to 8	0	0	0	0	0	1 (1.5%)	0	0	1 (1.6%)	2 (0.3%)	2 (0.3%)
Week 9 to 16	1 (0.8%)	0	0	3 (4.7%)	0	0	1 (1.6%)	0	1 (1.6%)	5 (0.9%)	6 (0.8%)
Week 17 to 24	1 (0.8%)	2 (1.6%)	0	0	0	0	0	1 (1.4%)	0	3 (0.5%)	4 (0.6%)
Week 25 to 32	0	0	0	1 (1.6%)	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 33 to 40	0	0	0	0	0	0	0	0	0	0	0
Week 41 to 48	0	0	1 (1.7%)	2 (3.3%)	0	0	0	1 (1.4%)	0	4 (0.7%)	4 (0.6%)
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Constipation (便秘)											
Week 1 to 4	3 (2.2%)	2 (1.6%)	1 (1.6%)	0	0	0	1 (1.6%)	0	0	4 (0.7%)	7 (1.0%)
Week 5 to 8	2 (1.5%)	0	0	1 (1.6%)	0	1 (1.5%)	1 (1.6%)	0	0	3 (0.5%)	5 (0.7%)
Week 9 to 16	0	5 (4.0%)	1 (1.6%)	0	0	0	1 (1.6%)	0	2 (3.2%)	9 (1.6%)	9 (1.3%)
Week 17 to 24	0	1 (0.8%)	0	0	1 (1.6%)	0	1 (1.6%)	1 (1.4%)	0	4 (0.7%)	4 (0.6%)
Week 25 to 32	0	1 (0.8%)	0	0	0	0	1 (1.6%)	0	0	2 (0.4%)	2 (0.3%)
Week 33 to 40	1 (0.8%)	0	0	0	1 (1.6%)	0	0	0	1 (1.6%)	2 (0.4%)	3 (0.4%)
Week 41 to 48	0	0	1 (1.7%)	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Gastrooesophageal reflux disease (胃食道逆流性疾患)											
Week 1 to 4	0	3 (2.4%)	0	0	0	0	0	0	0	3 (0.5%)	3 (0.4%)
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	0	0	0	1 (1.6%)	0	0	0	1 (1.4%)	0	2 (0.3%)	2 (0.3%)
Week 17 to 24	0	4 (3.3%)	1 (1.6%)	1 (1.6%)	0	0	0	0	0	6 (1.0%)	6 (0.9%)
Week 25 to 32	1 (0.8%)	0	0	0	0	0	0	0	0	0	1 (0.1%)

System Organ Class Preferred Term Time Period	Imeglimin N = 134	Imeglimin + SU N = 127	Imeglimin + GLIN N = 64	Imeglimin + BIG N = 64	Imeglimin + AGI N = 64	Imeglimin + TZD N = 65	Imeglimin + DPP4-I N = 63	Imeglimin + GLP1-RA N = 70	Imeglimin + SGLT2-I N = 63	Combination Total N = 580	Imeglimin Total N = 714
Week 33 to 40	2 (1.6%)	0	0	0	0	0	0	0	0	0	2 (0.3%)
Week 41 to 48	0	2 (1.7%)	0	0	0	0	0	0	0	2 (0.4%)	2 (0.3%)
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Abdominal pain upper (上腹部痛)											
Week 1 to 4	0	1 (0.8%)	0	2 (3.1%)	0	0	0	1 (1.4%)	0	4 (0.7%)	4 (0.6%)
Week 5 to 8	1 (0.7%)	0	0	1 (1.6%)	0	0	0	0	0	1 (0.2%)	2 (0.3%)
Week 9 to 16	0	1 (0.8%)	0	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 17 to 24	0	1 (0.8%)	0	1 (1.6%)	0	0	0	0	0	2 (0.3%)	2 (0.3%)
Week 25 to 32	1 (0.8%)	1 (0.8%)	0	0	0	0	0	0	0	1 (0.2%)	2 (0.3%)
Week 33 to 40	0	0	0	0	0	0	1 (1.6%)	0	0	1 (0.2%)	1 (0.1%)
Week 41 to 48	2 (1.6%)	0	1 (1.7%)	0	0	0	1 (1.7%)	0	0	2 (0.4%)	4 (0.6%)
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Dental caries (齲歯)											
Week 1 to 4	1 (0.7%)	0	0	0	0	1 (1.5%)	0	0	0	1 (0.2%)	2 (0.3%)
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	2 (1.5%)	0	1 (1.6%)	1 (1.6%)	0	0	1 (1.6%)	0	0	3 (0.5%)	5 (0.7%)
Week 17 to 24	1 (0.8%)	0	0	0	0	0	0	0	0	0	1 (0.1%)
Week 25 to 32	0	0	0	0	0	1 (1.5%)	0	0	0	1 (0.2%)	1 (0.1%)
Week 33 to 40	1 (0.8%)	0	0	0	0	0	1 (1.6%)	0	0	1 (0.2%)	2 (0.3%)
Week 41 to 48	1 (0.8%)	0	0	0	0	1 (1.5%)	0	0	0	1 (0.2%)	2 (0.3%)
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Vomiting (嘔吐)											
Week 1 to 4	0	0	0	3 (4.7%)	0	2 (3.1%)	1 (1.6%)	1 (1.4%)	0	7 (1.2%)	7 (1.0%)
Week 5 to 8	0	0	0	1 (1.6%)	0	0	0	1 (1.4%)	0	2 (0.3%)	2 (0.3%)
Week 9 to 16	0	0	0	3 (4.7%)	0	0	0	0	0	3 (0.5%)	3 (0.4%)
Week 17 to 24	1 (0.8%)	0	0	0	0	0	0	0	0	0	1 (0.1%)
Week 25 to 32	0	0	0	0	0	0	1 (1.6%)	0	0	1 (0.2%)	1 (0.1%)

System Organ Class Preferred Term Time Period	Imeglimin N = 134	Imeglimin + SU N = 127	Imeglimin + GLIN N = 64	Imeglimin + BIG N = 64	Imeglimin + AGI N = 64	Imeglimin + TZD N = 65	Imeglimin + DPP4-I N = 63	Imeglimin + GLP1-RA N = 70	Imeglimin + SGLT2-I N = 63	Combination Total N = 580	Imeglimin Total N = 714
Week 33 to 40	0	0	0	0	0	0	0	0	0	0	0
Week 41 to 48	0	0	0	1 (1.7%)	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 49 or later	0	0	0	1 (1.7%)	0	0	0	0	1 (1.6%)	2 (0.4%)	2 (0.3%)
Abdominal discomfort (腹部不快感)											
Week 1 to 4	0	0	1 (1.6%)	3 (4.7%)	0	0	1 (1.6%)	0	0	5 (0.9%)	5 (0.7%)
Week 5 to 8	0	1 (0.8%)	0	0	1 (1.6%)	0	0	0	0	2 (0.3%)	2 (0.3%)
Week 9 to 16	0	1 (0.8%)	0	0	0	0	1 (1.6%)	0	0	2 (0.3%)	2 (0.3%)
Week 17 to 24	0	0	0	0	0	0	0	0	0	0	0
Week 25 to 32	0	0	0	0	0	0	0	0	0	0	0
Week 33 to 40	0	0	0	0	0	0	0	0	0	0	0
Week 41 to 48	0	0	0	0	0	0	0	0	0	0	0
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Chronic gastritis (慢性胃炎)											
Week 1 to 4	0	0	0	0	0	0	1 (1.6%)	0	0	1 (0.2%)	1 (0.1%)
Week 5 to 8	0	0	0	0	0	0	0	0	1 (1.6%)	1 (0.2%)	1 (0.1%)
Week 9 to 16	0	0	0	0	0	0	0	1 (1.4%)	0	1 (0.2%)	1 (0.1%)
Week 17 to 24	0	2 (1.6%)	0	1 (1.6%)	0	0	0	0	0	3 (0.5%)	3 (0.4%)
Week 25 to 32	0	0	0	0	0	0	1 (1.6%)	0	0	1 (0.2%)	1 (0.1%)
Week 33 to 40	0	0	0	0	0	0	0	0	0	0	0
Week 41 to 48	0	0	0	0	0	0	0	0	0	0	0
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Dyspepsia (消化不良)											
Week 1 to 4	0	0	0	0	0	0	1 (1.6%)	2 (2.9%)	0	3 (0.5%)	3 (0.4%)
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	0	1 (0.8%)	1 (1.6%)	0	0	0	0	0	0	2 (0.3%)	2 (0.3%)
Week 17 to 24	0	1 (0.8%)	0	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 25 to 32	0	0	0	0	0	0	1 (1.6%)	0	0	1 (0.2%)	1 (0.1%)

System Organ Class Preferred Term Time Period	Imeglimin N = 134	Imeglimin + SU N = 127	Imeglimin + GLIN N = 64	Imeglimin + BIG N = 64	Imeglimin + AGI N = 64	Imeglimin + TZD N = 65	Imeglimin + DPP4-I N = 63	Imeglimin + GLP1-RA N = 70	Imeglimin + SGLT2-I N = 63	Combination Total N = 580	Imeglimin Total N = 714
Week 33 to 40	0	0	0	0	0	0	0	0	0	0	0
Week 41 to 48	0	0	0	0	0	0	0	0	0	0	0
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Faeces soft (軟便)											
Week 1 to 4	1 (0.7%)	1 (0.8%)	0	1 (1.6%)	0	0	0	0	0	2 (0.3%)	3 (0.4%)
Week 5 to 8	0	0	0	0	0	0	0	0	1 (1.6%)	1 (0.2%)	1 (0.1%)
Week 9 to 16	0	0	0	1 (1.6%)	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 17 to 24	0	0	1 (1.6%)	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 25 to 32	0	0	0	0	0	0	0	0	0	0	0
Week 33 to 40	0	0	0	0	0	0	0	0	0	0	0
Week 41 to 48	0	0	0	0	0	0	0	0	0	0	0
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Large intestine polyp (大腸ポリープ)											
Week 1 to 4	0	0	0	0	0	0	0	0	1 (1.6%)	1 (0.2%)	1 (0.1%)
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	0	0	0	0	0	0	0	1 (1.4%)	0	1 (0.2%)	1 (0.1%)
Week 17 to 24	1 (0.8%)	0	0	0	0	0	1 (1.6%)	0	0	1 (0.2%)	2 (0.3%)
Week 25 to 32	0	0	0	1 (1.6%)	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 33 to 40	0	0	0	0	0	0	1 (1.6%)	0	0	1 (0.2%)	1 (0.1%)
Week 41 to 48	0	0	0	1 (1.7%)	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Gastritis (胃炎)											
Week 1 to 4	0	0	0	0	1 (1.6%)	0	0	0	1 (1.6%)	2 (0.3%)	2 (0.3%)
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	0	0	0	0	0	0	0	0	0	0	0
Week 17 to 24	0	0	0	0	0	0	0	0	2 (3.2%)	2 (0.3%)	2 (0.3%)
Week 25 to 32	0	0	0	0	0	0	0	0	0	0	0

System Organ Class Preferred Term Time Period	Imeglimin N = 134	Imeglimin + SU N = 127	Imeglimin + GLIN N = 64	Imeglimin + BIG N = 64	Imeglimin + AGI N = 64	Imeglimin + TZD N = 65	Imeglimin + DPP4-I N = 63	Imeglimin + GLP1-RA N = 70	Imeglimin + SGLT2-I N = 63	Combination Total N = 580	Imeglimin Total N = 714
Week 33 to 40	0	0	0	0	0	0	0	1 (1.4%)	0	1 (0.2%)	1 (0.1%)
Week 41 to 48	0	0	0	0	0	0	0	0	0	0	0
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Abdominal distension (腹部膨満)											
Week 1 to 4	0	0	0	0	0	0	1 (1.6%)	0	1 (1.6%)	2 (0.3%)	2 (0.3%)
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	0	0	0	0	0	0	0	0	0	0	0
Week 17 to 24	0	0	0	0	0	0	0	0	0	0	0
Week 25 to 32	0	0	0	0	0	0	0	0	0	0	0
Week 33 to 40	0	0	0	0	0	0	0	0	1 (1.6%)	1 (0.2%)	1 (0.1%)
Week 41 to 48	0	0	0	0	0	0	0	0	0	0	0
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Metabolism and nutrition disorders (代謝および栄養障害)											
Hypoglycaemia (低血糖)											
Week 1 to 4	1 (0.7%)	5 (3.9%)	0	1 (1.6%)	0	0	0	0	0	6 (1.0%)	7 (1.0%)
Week 5 to 8	0	2 (1.6%)	2 (3.2%)	0	0	0	0	0	1 (1.6%)	5 (0.9%)	5 (0.7%)
Week 9 to 16	3 (2.3%)	6 (4.8%)	1 (1.6%)	0	0	0	2 (3.2%)	0	1 (1.6%)	10 (1.7%)	13 (1.8%)
Week 17 to 24	0	5 (4.1%)	4 (6.3%)	1 (1.6%)	1 (1.6%)	0	1 (1.6%)	0	1 (1.6%)	13 (2.3%)	13 (1.8%)
Week 25 to 32	1 (0.8%)	9 (7.3%)	3 (4.8%)	1 (1.6%)	1 (1.6%)	0	0	0	1 (1.6%)	15 (2.6%)	16 (2.3%)
Week 33 to 40	0	4 (3.3%)	2 (3.3%)	0	0	2 (3.1%)	1 (1.6%)	2 (2.9%)	0	11 (1.9%)	11 (1.6%)
Week 41 to 48	1 (0.8%)	5 (4.2%)	3 (5.0%)	2 (3.3%)	1 (1.6%)	0	2 (3.3%)	0	0	13 (2.3%)	14 (2.0%)
Week 49 or later	0	2 (1.7%)	2 (3.3%)	1 (1.7%)	0	0	0	0	0	5 (0.9%)	5 (0.7%)
Hyperglycaemia (高血糖)											
Week 1 to 4	0	0	0	0	0	0	0	0	0	0	0
Week 5 to 8	0	1 (0.8%)	0	0	0	0	1 (1.6%)	2 (2.9%)	0	4 (0.7%)	4 (0.6%)

System Organ Class Preferred Term Time Period	Imeglimin N = 134	Imeglimin + SU N = 127	Imeglimin + GLIN N = 64	Imeglimin + BIG N = 64	Imeglimin + AGI N = 64	Imeglimin + TZD N = 65	Imeglimin + DPP4-I N = 63	Imeglimin + GLP1-RA N = 70	Imeglimin + SGLT2-I N = 63	Combination Total N = 580	Imeglimin Total N = 714
Week 9 to 16	0	1 (0.8%)	0	0	0	0	0	2 (2.9%)	0	3 (0.5%)	3 (0.4%)
Week 17 to 24	1 (0.8%)	1 (0.8%)	0	0	0	0	0	1 (1.4%)	1 (1.6%)	3 (0.5%)	4 (0.6%)
Week 25 to 32	0	1 (0.8%)	0	0	0	0	0	2 (2.9%)	0	3 (0.5%)	3 (0.4%)
Week 33 to 40	0	1 (0.8%)	0	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 41 to 48	2 (1.6%)	2 (1.7%)	0	0	1 (1.6%)	1 (1.5%)	0	1 (1.4%)	0	5 (0.9%)	7 (1.0%)
Week 49 or later	2 (1.6%)	0	0	0	0	0	1 (1.7%)	0	0	1 (0.2%)	3 (0.4%)
Decreased appetite (食欲減退)											
Week 1 to 4	0	0	0	0	0	1 (1.5%)	2 (3.2%)	0	0	3 (0.5%)	3 (0.4%)
Week 5 to 8	1 (0.7%)	0	0	1 (1.6%)	0	0	0	3 (4.3%)	1 (1.6%)	5 (0.9%)	6 (0.8%)
Week 9 to 16	1 (0.8%)	0	0	0	0	0	0	0	0	0	1 (0.1%)
Week 17 to 24	1 (0.8%)	0	0	1 (1.6%)	0	0	0	0	0	1 (0.2%)	2 (0.3%)
Week 25 to 32	0	0	0	0	0	0	0	0	0	0	0
Week 33 to 40	0	0	0	0	0	0	0	0	0	0	0
Week 41 to 48	0	0	0	0	0	0	0	0	0	0	0
Week 49 or later	0	0	0	0	0	1 (1.5%)	0	0	0	1 (0.2%)	1 (0.1%)
Musculoskeletal and connective tissue disorders (筋骨格系および結合組織障害)											
Back pain (背部痛)											
Week 1 to 4	0	0	0	0	0	0	0	0	0	0	0
Week 5 to 8	0	2 (1.6%)	1 (1.6%)	0	0	0	0	0	0	3 (0.5%)	3 (0.4%)
Week 9 to 16	1 (0.8%)	1 (0.8%)	1 (1.6%)	1 (1.6%)	0	0	1 (1.6%)	0	0	4 (0.7%)	5 (0.7%)
Week 17 to 24	2 (1.5%)	2 (1.6%)	0	1 (1.6%)	2 (3.1%)	1 (1.5%)	1 (1.6%)	0	0	7 (1.2%)	9 (1.3%)
Week 25 to 32	2 (1.5%)	2 (1.6%)	1 (1.6%)	0	0	2 (3.1%)	0	0	0	5 (0.9%)	7 (1.0%)
Week 33 to 40	0	1 (0.8%)	0	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 41 to 48	0	0	0	0	0	1 (1.5%)	0	0	0	1 (0.2%)	1 (0.1%)
Week 49 or later	1 (0.8%)	2 (1.7%)	0	0	0	0	0	0	0	2 (0.4%)	3 (0.4%)

System Organ Class Preferred Term Time Period	Imeglimin N = 134	Imeglimin + SU N = 127	Imeglimin + GLIN N = 64	Imeglimin + BIG N = 64	Imeglimin + AGI N = 64	Imeglimin + TZD N = 65	Imeglimin + DPP4-I N = 63	Imeglimin + GLP1-RA N = 70	Imeglimin + SGLT2-I N = 63	Combination Total N = 580	Imeglimin Total N = 714
Arthralgia (関節痛)											
Week 1 to 4	0	1 (0.8%)	0	1 (1.6%)	0	0	0	0	0	2 (0.3%)	2 (0.3%)
Week 5 to 8	1 (0.7%)	0	0	0	0	0	0	0	0	0	1 (0.1%)
Week 9 to 16	0	0	0	0	0	0	0	2 (2.9%)	0	2 (0.3%)	2 (0.3%)
Week 17 to 24	0	0	0	1 (1.6%)	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 25 to 32	0	0	0	0	0	0	1 (1.6%)	0	1 (1.6%)	2 (0.4%)	2 (0.3%)
Week 33 to 40	0	2 (1.6%)	0	0	0	1 (1.5%)	1 (1.6%)	0	0	4 (0.7%)	4 (0.6%)
Week 41 to 48	0	0	0	0	0	1 (1.5%)	0	0	0	1 (0.2%)	1 (0.1%)
Week 49 or later	0	0	0	0	0	0	0	0	1 (1.6%)	1 (0.2%)	1 (0.1%)
Pain in extremity (四肢痛)											
Week 1 to 4	0	0	1 (1.6%)	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	0	0	0	0	0	0	0	0	0	0	0
Week 17 to 24	1 (0.8%)	1 (0.8%)	1 (1.6%)	0	0	0	0	0	0	2 (0.3%)	3 (0.4%)
Week 25 to 32	0	2 (1.6%)	0	0	0	0	1 (1.6%)	0	0	3 (0.5%)	3 (0.4%)
Week 33 to 40	0	0	0	0	0	0	0	1 (1.4%)	0	1 (0.2%)	1 (0.1%)
Week 41 to 48	0	0	0	0	0	0	0	0	1 (1.6%)	1 (0.2%)	1 (0.1%)
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Myalgia (筋肉痛)											
Week 1 to 4	0	0	0	1 (1.6%)	0	0	0	0	1 (1.6%)	2 (0.3%)	2 (0.3%)
Week 5 to 8	0	1 (0.8%)	0	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 9 to 16	0	0	0	1 (1.6%)	1 (1.6%)	0	0	0	0	2 (0.3%)	2 (0.3%)
Week 17 to 24	0	0	0	0	0	0	0	0	0	0	0
Week 25 to 32	1 (0.8%)	0	1 (1.6%)	0	0	0	0	0	0	1 (0.2%)	2 (0.3%)
Week 33 to 40	1 (0.8%)	0	0	0	0	0	0	0	0	0	1 (0.1%)
Week 41 to 48	0	0	0	0	0	0	0	0	0	0	0
Week 49 or later	0	0	0	0	0	0	0	0	1 (1.6%)	1 (0.2%)	1 (0.1%)

System Organ Class Preferred Term Time Period	Imeglimin N = 134	Imeglimin + SU N = 127	Imeglimin + GLIN N = 64	Imeglimin + BIG N = 64	Imeglimin + AGI N = 64	Imeglimin + TZD N = 65	Imeglimin + DPP4-I N = 63	Imeglimin + GLP1-RA N = 70	Imeglimin + SGLT2-I N = 63	Combination Total N = 580	Imeglimin Total N = 714
Spinal osteoarthritis (変形性脊椎症)											
Week 1 to 4	0	0	0	0	1 (1.6%)	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 5 to 8	1 (0.7%)	0	0	0	0	0	0	0	0	0	1 (0.1%)
Week 9 to 16	0	0	0	0	0	0	1 (1.6%)	0	0	1 (0.2%)	1 (0.1%)
Week 17 to 24	0	0	0	0	0	0	0	0	0	0	0
Week 25 to 32	0	0	0	0	0	0	1 (1.6%)	0	0	1 (0.2%)	1 (0.1%)
Week 33 to 40	0	0	0	0	0	0	1 (1.6%)	1 (1.4%)	1 (1.6%)	3 (0.5%)	3 (0.4%)
Week 41 to 48	0	0	0	0	0	0	0	0	0	0	0
Week 49 or later	0	0	0	0	0	0	1 (1.7%)	0	0	1 (0.2%)	1 (0.1%)
Intervertebral disc protrusion (椎間板突出)											
Week 1 to 4	0	0	0	0	0	0	0	0	0	0	0
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	0	0	0	0	0	0	2 (3.2%)	0	0	2 (0.3%)	2 (0.3%)
Week 17 to 24	0	0	0	0	0	0	1 (1.6%)	1 (1.4%)	0	2 (0.3%)	2 (0.3%)
Week 25 to 32	0	0	0	0	0	0	1 (1.6%)	0	0	1 (0.2%)	1 (0.1%)
Week 33 to 40	0	0	0	0	1 (1.6%)	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 41 to 48	0	0	0	0	0	0	0	0	0	0	0
Week 49 or later	0	0	1 (1.7%)	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Osteoarthritis (変形性関節症)											
Week 1 to 4	1 (0.7%)	0	0	0	0	0	0	0	0	0	1 (0.1%)
Week 5 to 8	0	0	1 (1.6%)	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 9 to 16	1 (0.8%)	0	0	1 (1.6%)	0	0	0	0	0	1 (0.2%)	2 (0.3%)
Week 17 to 24	0	0	0	0	0	0	1 (1.6%)	0	0	1 (0.2%)	1 (0.1%)
Week 25 to 32	0	0	0	0	0	0	0	0	0	0	0
Week 33 to 40	0	0	0	0	0	0	1 (1.6%)	0	0	1 (0.2%)	1 (0.1%)
Week 41 to 48	0	0	0	0	0	0	0	0	0	0	0

System Organ Class Preferred Term Time Period	Imeglimin N = 134	Imeglimin + SU N = 127	Imeglimin + GLIN N = 64	Imeglimin + BIG N = 64	Imeglimin + AGI N = 64	Imeglimin + TZD N = 65	Imeglimin + DPP4-I N = 63	Imeglimin + GLP1-RA N = 70	Imeglimin + SGLT2-I N = 63	Combination Total N = 580	Imeglimin Total N = 714
Week 49 or later	0	0	0	0	0	0	1 (1.7%)	0	0	1 (0.2%)	1 (0.1%)
Lumbar spinal stenosis (腰部脊柱管狭窄症)											
Week 1 to 4	0	0	0	0	0	0	0	0	0	0	0
Week 5 to 8	1 (0.7%)	0	0	0	0	0	0	0	0	0	1 (0.1%)
Week 9 to 16	0	0	0	0	0	0	0	0	0	0	0
Week 17 to 24	0	0	0	0	0	0	0	0	0	0	0
Week 25 to 32	0	0	0	0	0	0	1 (1.6%)	1 (1.4%)	0	2 (0.4%)	2 (0.3%)
Week 33 to 40	0	0	0	0	0	0	0	1 (1.4%)	0	1 (0.2%)	1 (0.1%)
Week 41 to 48	0	0	0	0	0	0	0	1 (1.4%)	0	1 (0.2%)	1 (0.1%)
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Muscle spasms (筋痙縮)											
Week 1 to 4	0	0	0	0	0	0	0	0	0	0	0
Week 5 to 8	0	0	1 (1.6%)	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 9 to 16	0	0	1 (1.6%)	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 17 to 24	0	0	0	0	0	0	0	0	0	0	0
Week 25 to 32	0	1 (0.8%)	0	0	0	0	1 (1.6%)	0	0	2 (0.4%)	2 (0.3%)
Week 33 to 40	0	0	0	0	0	0	0	0	0	0	0
Week 41 to 48	0	0	0	0	0	0	0	0	0	0	0
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Musculoskeletal stiffness (筋骨格硬直)											
Week 1 to 4	0	0	0	0	0	0	0	0	0	0	0
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	0	1 (0.8%)	0	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 17 to 24	0	0	0	0	0	0	0	0	0	0	0
Week 25 to 32	0	1 (0.8%)	0	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 33 to 40	0	0	1 (1.6%)	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)

System Organ Class Preferred Term Time Period	Imeglimin N = 134	Imeglimin + SU N = 127	Imeglimin + GLIN N = 64	Imeglimin + BIG N = 64	Imeglimin + AGI N = 64	Imeglimin + TZD N = 65	Imeglimin + DPP4-I N = 63	Imeglimin + GLP1-RA N = 70	Imeglimin + SGLT2-I N = 63	Combination Total N = 580	Imeglimin Total N = 714
Week 41 to 48	0	0	1 (1.7%)	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Trigger finger (弾発指)											
Week 1 to 4	0	0	0	0	0	0	1 (1.6%)	0	0	1 (0.2%)	1 (0.1%)
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	0	0	0	0	0	0	0	0	0	0	0
Week 17 to 24	0	0	0	0	0	0	0	0	0	0	0
Week 25 to 32	0	0	0	0	0	0	0	1 (1.4%)	0	1 (0.2%)	1 (0.1%)
Week 33 to 40	0	0	0	0	0	0	0	1 (1.4%)	0	1 (0.2%)	1 (0.1%)
Week 41 to 48	0	0	0	0	0	0	1 (1.7%)	0	0	1 (0.2%)	1 (0.1%)
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Skin and subcutaneous tissue disorders (皮膚および皮下組織障害)											
Eczema (湿疹)											
Week 1 to 4	0	0	1 (1.6%)	0	0	0	1 (1.6%)	0	0	2 (0.3%)	2 (0.3%)
Week 5 to 8	1 (0.7%)	0	0	0	0	0	1 (1.6%)	1 (1.4%)	0	2 (0.3%)	3 (0.4%)
Week 9 to 16	1 (0.8%)	1 (0.8%)	0	0	0	0	1 (1.6%)	1 (1.4%)	1 (1.6%)	4 (0.7%)	5 (0.7%)
Week 17 to 24	0	1 (0.8%)	2 (3.2%)	0	0	0	1 (1.6%)	0	0	4 (0.7%)	4 (0.6%)
Week 25 to 32	0	0	0	0	0	1 (1.5%)	1 (1.6%)	2 (2.9%)	0	4 (0.7%)	4 (0.6%)
Week 33 to 40	0	1 (0.8%)	0	0	0	0	0	0	1 (1.6%)	2 (0.4%)	2 (0.3%)
Week 41 to 48	0	1 (0.8%)	0	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Acne (ざ瘡)											
Week 1 to 4	0	0	0	1 (1.6%)	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	0	1 (0.8%)	0	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)

System Organ Class Preferred Term Time Period	Imeglimin N = 134	Imeglimin + SU N = 127	Imeglimin + GLIN N = 64	Imeglimin + BIG N = 64	Imeglimin + AGI N = 64	Imeglimin + TZD N = 65	Imeglimin + DPP4-I N = 63	Imeglimin + GLP1-RA N = 70	Imeglimin + SGLT2-I N = 63	Combination Total N = 580	Imeglimin Total N = 714
Week 17 to 24	0	0	1 (1.6%)	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 25 to 32	0	0	0	0	0	0	0	0	0	0	0
Week 33 to 40	0	0	0	0	0	0	0	0	0	0	0
Week 41 to 48	0	0	1 (1.7%)	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Hyperkeratosis (過角化)											
Week 1 to 4	0	0	0	0	0	0	0	0	0	0	0
Week 5 to 8	0	1 (0.8%)	0	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 9 to 16	0	0	0	0	0	0	0	0	0	0	0
Week 17 to 24	0	0	0	0	0	0	0	0	1 (1.6%)	1 (0.2%)	1 (0.1%)
Week 25 to 32	0	0	0	0	0	0	0	0	0	0	0
Week 33 to 40	0	0	0	0	0	0	0	0	1 (1.6%)	1 (0.2%)	1 (0.1%)
Week 41 to 48	0	0	0	0	0	0	0	0	0	0	0
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Injury, poisoning and procedural complications (傷害、中毒および処置合併症)											
Contusion (挫傷)											
Week 1 to 4	0	0	0	1 (1.6%)	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 5 to 8	0	0	0	0	0	0	1 (1.6%)	0	0	1 (0.2%)	1 (0.1%)
Week 9 to 16	0	0	0	0	0	0	0	0	0	0	0
Week 17 to 24	2 (1.5%)	0	0	0	0	0	0	0	0	0	2 (0.3%)
Week 25 to 32	0	1 (0.8%)	0	0	0	0	1 (1.6%)	0	0	2 (0.4%)	2 (0.3%)
Week 33 to 40	0	1 (0.8%)	0	1 (1.7%)	0	0	0	0	0	2 (0.4%)	2 (0.3%)
Week 41 to 48	1 (0.8%)	1 (0.8%)	0	0	0	0	1 (1.7%)	0	0	2 (0.4%)	3 (0.4%)
Week 49 or later	0	0	0	0	0	0	1 (1.7%)	0	0	1 (0.2%)	1 (0.1%)
Ligament sprain (靱帯捻挫)											

System Organ Class Preferred Term Time Period	Imeglimin N = 134	Imeglimin + SU N = 127	Imeglimin + GLIN N = 64	Imeglimin + BIG N = 64	Imeglimin + AGI N = 64	Imeglimin + TZD N = 65	Imeglimin + DPP4-I N = 63	Imeglimin + GLP1-RA N = 70	Imeglimin + SGLT2-I N = 63	Combination Total N = 580	Imeglimin Total N = 714
Week 1 to 4	0	0	1 (1.6%)	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	0	0	1 (1.6%)	0	0	1 (1.5%)	0	1 (1.4%)	0	3 (0.5%)	3 (0.4%)
Week 17 to 24	0	0	0	0	0	0	0	0	0	0	0
Week 25 to 32	1 (0.8%)	0	0	0	0	0	0	0	0	0	1 (0.1%)
Week 33 to 40	0	1 (0.8%)	0	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 41 to 48	0	0	0	0	0	0	0	0	0	0	0
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Thermal burn (熱傷)											
Week 1 to 4	0	0	0	0	0	0	0	0	0	0	0
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	0	0	0	2 (3.1%)	0	0	0	0	0	2 (0.3%)	2 (0.3%)
Week 17 to 24	0	0	0	0	0	0	1 (1.6%)	0	0	1 (0.2%)	1 (0.1%)
Week 25 to 32	0	0	0	0	0	0	0	1 (1.4%)	0	1 (0.2%)	1 (0.1%)
Week 33 to 40	1 (0.8%)	0	0	0	0	0	0	0	0	0	1 (0.1%)
Week 41 to 48	0	0	0	0	0	0	0	0	0	0	0
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Radius fracture (橈骨骨折)											
Week 1 to 4	0	0	0	0	0	0	0	0	0	0	0
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	0	0	0	0	0	0	1 (1.6%)	0	0	1 (0.2%)	1 (0.1%)
Week 17 to 24	0	0	0	0	0	0	0	0	0	0	0
Week 25 to 32	0	0	0	0	0	0	0	0	0	0	0
Week 33 to 40	0	0	0	0	0	0	0	0	0	0	0
Week 41 to 48	0	0	0	0	0	0	0	0	0	0	0
Week 49 or later	1 (0.8%)	0	0	0	0	0	1 (1.7%)	0	0	1 (0.2%)	2 (0.3%)
Tendon rupture (腱断裂)											
Week 1 to 4	0	0	0	0	0	0	0	0	0	0	0
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0

System Organ Class Preferred Term Time Period	Imeglimin N = 134	Imeglimin + SU N = 127	Imeglimin + GLIN N = 64	Imeglimin + BIG N = 64	Imeglimin + AGI N = 64	Imeglimin + TZD N = 65	Imeglimin + DPP4-I N = 63	Imeglimin + GLP1-RA N = 70	Imeglimin + SGLT2-I N = 63	Combination Total N = 580	Imeglimin Total N = 714
Week 9 to 16	0	0	0	0	0	0	0	0	0	0	0
Week 17 to 24	0	0	0	0	0	0	0	0	0	0	0
Week 25 to 32	0	0	1 (1.6%)	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 33 to 40	0	0	1 (1.6%)	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 41 to 48	0	0	0	0	0	0	0	0	0	0	0
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Nervous system disorders (神経系障害)											
Headache (頭痛)											
Week 1 to 4	0	0	0	0	0	0	0	0	0	0	0
Week 5 to 8	0	0	0	0	0	1 (1.5%)	0	0	0	1 (0.2%)	1 (0.1%)
Week 9 to 16	1 (0.8%)	0	0	0	0	0	0	0	0	0	1 (0.1%)
Week 17 to 24	1 (0.8%)	0	1 (1.6%)	0	1 (1.6%)	0	0	0	0	2 (0.3%)	3 (0.4%)
Week 25 to 32	0	0	0	0	0	0	0	0	1 (1.6%)	1 (0.2%)	1 (0.1%)
Week 33 to 40	0	1 (0.8%)	0	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 41 to 48	0	0	0	0	0	0	0	0	0	0	0
Week 49 or later	0	0	0	0	0	1 (1.5%)	0	0	0	1 (0.2%)	1 (0.1%)
Diabetic neuropathy (糖尿病性ニューロパチー)											
Week 1 to 4	0	0	0	0	0	0	0	1 (1.4%)	0	1 (0.2%)	1 (0.1%)
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	0	0	0	0	0	0	1 (1.6%)	0	0	1 (0.2%)	1 (0.1%)
Week 17 to 24	1 (0.8%)	0	0	0	0	0	0	1 (1.4%)	1 (1.6%)	2 (0.3%)	3 (0.4%)
Week 25 to 32	0	0	0	0	0	0	1 (1.6%)	0	0	1 (0.2%)	1 (0.1%)
Week 33 to 40	0	0	0	0	0	0	0	0	0	0	0
Week 41 to 48	0	0	0	0	0	0	0	0	0	0	0
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0

System Organ Class Preferred Term Time Period	Imeglimin N = 134	Imeglimin + SU N = 127	Imeglimin + GLIN N = 64	Imeglimin + BIG N = 64	Imeglimin + AGI N = 64	Imeglimin + TZD N = 65	Imeglimin + DPP4-I N = 63	Imeglimin + GLP1-RA N = 70	Imeglimin + SGLT2-I N = 63	Combination Total N = 580	Imeglimin Total N = 714
Carotid arteriosclerosis (頚動脈硬化症)											
Week 1 to 4	0	0	0	0	0	0	0	0	0	0	0
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	0	0	0	0	0	0	0	0	0	0	0
Week 17 to 24	0	0	0	0	0	0	0	0	0	0	0
Week 25 to 32	0	0	0	0	0	0	0	0	0	0	0
Week 33 to 40	0	0	0	0	0	0	0	0	0	0	0
Week 41 to 48	0	0	0	1 (1.7%)	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 49 or later	0	0	1 (1.7%)	0	0	2 (3.1%)	0	0	0	3 (0.5%)	3 (0.4%)
Cervicobrachial syndrome (頚腕症候群)											
Week 1 to 4	0	0	0	0	0	0	0	0	0	0	0
Week 5 to 8	0	0	0	0	1 (1.6%)	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 9 to 16	1 (0.8%)	0	0	0	0	0	0	0	0	0	1 (0.1%)
Week 17 to 24	0	0	0	0	1 (1.6%)	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 25 to 32	0	0	0	0	0	0	0	0	0	0	0
Week 33 to 40	0	0	0	0	0	0	0	0	0	0	0
Week 41 to 48	0	0	0	0	0	0	0	0	0	0	0
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Intercostal neuralgia (肋間神経痛)											
Week 1 to 4	0	0	0	0	0	0	0	0	0	0	0
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	0	0	2 (3.2%)	0	0	0	0	0	0	2 (0.3%)	2 (0.3%)
Week 17 to 24	0	0	0	0	0	0	0	0	0	0	0
Week 25 to 32	0	0	0	0	0	0	0	0	0	0	0
Week 33 to 40	0	0	0	0	0	0	0	0	0	0	0

System Organ Class Preferred Term Time Period	Imeglimin N = 134	Imeglimin + SU N = 127	Imeglimin + GLIN N = 64	Imeglimin + BIG N = 64	Imeglimin + AGI N = 64	Imeglimin + TZD N = 65	Imeglimin + DPP4-I N = 63	Imeglimin + GLP1-RA N = 70	Imeglimin + SGLT2-I N = 63	Combination Total N = 580	Imeglimin Total N = 714
Week 41 to 48	0	0	1 (1.7%)	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Respiratory, thoracic and mediastinal disorders (呼吸器、胸郭および縦隔障害)											
Upper respiratory tract inflammation (上気道の炎症)											
Week 1 to 4	0	0	0	0	0	0	0	0	1 (1.6%)	1 (0.2%)	1 (0.1%)
Week 5 to 8	0	0	1 (1.6%)	0	0	0	1 (1.6%)	0	0	2 (0.3%)	2 (0.3%)
Week 9 to 16	1 (0.8%)	0	0	0	0	0	1 (1.6%)	0	1 (1.6%)	2 (0.3%)	3 (0.4%)
Week 17 to 24	0	0	0	0	1 (1.6%)	0	0	0	2 (3.2%)	3 (0.5%)	3 (0.4%)
Week 25 to 32	0	1 (0.8%)	1 (1.6%)	0	0	0	1 (1.6%)	0	0	3 (0.5%)	3 (0.4%)
Week 33 to 40	0	0	0	0	0	1 (1.5%)	1 (1.6%)	0	0	2 (0.4%)	2 (0.3%)
Week 41 to 48	0	0	0	0	0	1 (1.5%)	1 (1.7%)	0	1 (1.6%)	3 (0.5%)	3 (0.4%)
Week 49 or later	0	0	0	0	0	0	2 (3.3%)	0	0	2 (0.4%)	2 (0.3%)
Cough (咳嗽)											
Week 1 to 4	0	0	0	0	0	0	0	0	0	0	0
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	1 (0.8%)	2 (1.6%)	0	0	0	0	0	0	0	2 (0.3%)	3 (0.4%)
Week 17 to 24	1 (0.8%)	0	1 (1.6%)	0	0	0	0	1 (1.4%)	0	2 (0.3%)	3 (0.4%)
Week 25 to 32	1 (0.8%)	0	0	0	0	1 (1.5%)	0	0	0	1 (0.2%)	2 (0.3%)
Week 33 to 40	0	0	0	0	0	0	0	0	0	0	0
Week 41 to 48	0	0	0	0	0	0	0	0	0	0	0
Week 49 or later	0	0	0	1 (1.7%)	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Vascular disorders (血管障害)											
Hypertension (高血圧)											

System Organ Class Preferred Term Time Period	Imeglimin N = 134	Imeglimin + SU N = 127	Imeglimin + GLIN N = 64	Imeglimin + BIG N = 64	Imeglimin + AGI N = 64	Imeglimin + TZD N = 65	Imeglimin + DPP4-I N = 63	Imeglimin + GLP1-RA N = 70	Imeglimin + SGLT2-I N = 63	Combination Total N = 580	Imeglimin Total N = 714
Week 1 to 4	0	1 (0.8%)	0	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 5 to 8	0	0	0	0	0	1 (1.5%)	0	1 (1.4%)	0	2 (0.3%)	2 (0.3%)
Week 9 to 16	0	0	0	0	0	0	0	0	0	0	0
Week 17 to 24	0	1 (0.8%)	1 (1.6%)	0	0	0	0	0	0	2 (0.3%)	2 (0.3%)
Week 25 to 32	0	3 (2.4%)	1 (1.6%)	0	2 (3.1%)	1 (1.5%)	0	0	0	7 (1.2%)	7 (1.0%)
Week 33 to 40	0	0	0	1 (1.7%)	0	0	0	0	1 (1.6%)	2 (0.4%)	2 (0.3%)
Week 41 to 48	0	0	0	0	0	1 (1.5%)	0	1 (1.4%)	0	2 (0.4%)	2 (0.3%)
Week 49 or later	0	2 (1.7%)	0	0	1 (1.6%)	0	1 (1.7%)	0	0	4 (0.7%)	4 (0.6%)
Renal and urinary disorders (腎および尿路障害)											
Diabetic nephropathy (糖尿病性腎症)											
Week 1 to 4	0	1 (0.8%)	0	0	2 (3.1%)	0	1 (1.6%)	0	1 (1.6%)	5 (0.9%)	5 (0.7%)
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	0	0	0	0	0	0	0	0	0	0	0
Week 17 to 24	0	0	0	0	0	0	0	0	0	0	0
Week 25 to 32	0	0	0	1 (1.6%)	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 33 to 40	0	0	0	0	0	0	0	0	0	0	0
Week 41 to 48	0	0	0	0	0	1 (1.5%)	0	0	0	1 (0.2%)	1 (0.1%)
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Nephrolithiasis (腎結石症)											
Week 1 to 4	0	0	0	0	1 (1.6%)	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 5 to 8	1 (0.7%)	0	0	0	0	0	0	0	0	0	1 (0.1%)
Week 9 to 16	0	0	0	0	1 (1.6%)	0	0	1 (1.4%)	0	2 (0.3%)	2 (0.3%)
Week 17 to 24	0	0	0	0	0	0	1 (1.6%)	0	0	1 (0.2%)	1 (0.1%)
Week 25 to 32	0	0	0	0	0	1 (1.5%)	0	0	0	1 (0.2%)	1 (0.1%)
Week 33 to 40	0	0	0	0	0	0	0	0	0	0	0

System Organ Class Preferred Term Time Period	Imeglimin N = 134	Imeglimin + SU N = 127	Imeglimin + GLIN N = 64	Imeglimin + BIG N = 64	Imeglimin + AGI N = 64	Imeglimin + TZD N = 65	Imeglimin + DPP4-I N = 63	Imeglimin + GLP1-RA N = 70	Imeglimin + SGLT2-I N = 63	Combination Total N = 580	Imeglimin Total N = 714
Week 41 to 48	0	0	0	0	0	1 (1.5%)	0	0	0	1 (0.2%)	1 (0.1%)
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Pollakiuria (頻尿)											
Week 1 to 4	0	0	0	0	0	0	0	0	0	0	0
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	0	0	0	0	0	0	0	0	0	0	0
Week 17 to 24	0	0	0	0	0	0	0	0	1 (1.6%)	1 (0.2%)	1 (0.1%)
Week 25 to 32	0	0	0	0	0	0	0	1 (1.4%)	0	1 (0.2%)	1 (0.1%)
Week 33 to 40	0	0	0	0	0	0	0	1 (1.4%)	0	1 (0.2%)	1 (0.1%)
Week 41 to 48	0	0	0	0	0	0	0	0	0	0	0
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Eye disorders (眼障害)											
Diabetic retinopathy (糖尿病網膜症)											
Week 1 to 4	0	0	0	0	0	0	0	1 (1.4%)	0	1 (0.2%)	1 (0.1%)
Week 5 to 8	0	0	1 (1.6%)	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 9 to 16	0	0	0	0	0	1 (1.5%)	0	0	0	1 (0.2%)	1 (0.1%)
Week 17 to 24	0	0	0	0	0	1 (1.5%)	1 (1.6%)	0	0	2 (0.3%)	2 (0.3%)
Week 25 to 32	1 (0.8%)	1 (0.8%)	0	0	0	0	1 (1.6%)	0	0	2 (0.4%)	3 (0.4%)
Week 33 to 40	0	0	0	0	0	0	1 (1.6%)	0	0	1 (0.2%)	1 (0.1%)
Week 41 to 48	1 (0.8%)	0	0	0	0	0	0	0	0	0	1 (0.1%)
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Asthenopia (眼精疲労)											
Week 1 to 4	0	0	0	0	0	0	0	1 (1.4%)	0	1 (0.2%)	1 (0.1%)
Week 5 to 8	0	0	1 (1.6%)	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 9 to 16	0	0	0	0	0	0	0	0	0	0	0
Week 17 to 24	0	1 (0.8%)	0	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)

System Organ Class Preferred Term Time Period	Imeglimin N = 134	Imeglimin + SU N = 127	Imeglimin + GLIN N = 64	Imeglimin + BIG N = 64	Imeglimin + AGI N = 64	Imeglimin + TZD N = 65	Imeglimin + DPP4-I N = 63	Imeglimin + GLP1-RA N = 70	Imeglimin + SGLT2-I N = 63	Combination Total N = 580	Imeglimin Total N = 714
Week 25 to 32	0	0	0	0	0	0	0	0	0	0	0
Week 33 to 40	0	0	0	0	0	0	0	0	0	0	0
Week 41 to 48	0	0	1 (1.7%)	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Psychiatric disorders (精神障害)											
Insomnia (不眠症)											
Week 1 to 4	0	1 (0.8%)	0	1 (1.6%)	0	0	1 (1.6%)	0	0	3 (0.5%)	3 (0.4%)
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	0	0	0	1 (1.6%)	0	0	1 (1.6%)	0	0	2 (0.3%)	2 (0.3%)
Week 17 to 24	0	0	0	0	0	0	0	0	0	0	0
Week 25 to 32	2 (1.5%)	0	0	0	0	0	0	0	1 (1.6%)	1 (0.2%)	3 (0.4%)
Week 33 to 40	0	0	0	0	0	0	0	0	0	0	0
Week 41 to 48	0	0	0	0	0	0	1 (1.7%)	1 (1.4%)	0	2 (0.4%)	2 (0.3%)
Week 49 or later	0	0	0	0	0	1 (1.5%)	0	0	0	1 (0.2%)	1 (0.1%)
Hepatobiliary disorders (肝胆道系障害)											
Hepatic steatosis (脂肪肝)											
Week 1 to 4	0	0	0	0	0	0	0	0	0	0	0
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	0	0	0	0	0	0	0	2 (2.9%)	0	2 (0.3%)	2 (0.3%)
Week 17 to 24	0	1 (0.8%)	1 (1.6%)	0	0	0	0	0	0	2 (0.3%)	2 (0.3%)
Week 25 to 32	0	0	0	0	0	1 (1.5%)	0	0	0	1 (0.2%)	1 (0.1%)
Week 33 to 40	0	0	0	0	0	0	0	0	0	0	0
Week 41 to 48	0	0	0	0	0	0	0	0	0	0	0
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0

System Organ Class Preferred Term Time Period	Imeglimin N = 134	Imeglimin + SU N = 127	Imeglimin + GLIN N = 64	Imeglimin + BIG N = 64	Imeglimin + AGI N = 64	Imeglimin + TZD N = 65	Imeglimin + DPP4-I N = 63	Imeglimin + GLP1-RA N = 70	Imeglimin + SGLT2-I N = 63	Combination Total N = 580	Imeglimin Total N = 714
Alcoholic liver disease (アルコール性肝疾患)											
Week 1 to 4	0	0	0	0	0	0	0	0	0	0	0
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	0	0	0	0	0	0	0	1 (1.4%)	0	1 (0.2%)	1 (0.1%)
Week 17 to 24	0	0	0	0	0	0	0	0	0	0	0
Week 25 to 32	0	1 (0.8%)	0	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 33 to 40	0	0	0	0	0	0	0	1 (1.4%)	0	1 (0.2%)	1 (0.1%)
Week 41 to 48	0	0	0	0	0	0	0	0	0	0	0
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Cholelithiasis (胆石症)											
Week 1 to 4	0	0	0	0	0	0	0	0	0	0	0
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	0	0	0	0	0	0	0	1 (1.4%)	0	1 (0.2%)	1 (0.1%)
Week 17 to 24	0	0	0	0	0	0	0	0	0	0	0
Week 25 to 32	0	0	0	0	0	0	0	1 (1.4%)	0	1 (0.2%)	1 (0.1%)
Week 33 to 40	0	0	0	0	0	0	0	0	0	0	0
Week 41 to 48	0	0	0	0	1 (1.6%)	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Gallbladder polyp (胆嚢ポリープ)											
Week 1 to 4	0	0	0	0	0	0	0	0	0	0	0
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	0	0	0	0	0	0	0	2 (2.9%)	0	2 (0.3%)	2 (0.3%)
Week 17 to 24	0	0	0	0	0	0	0	0	0	0	0
Week 25 to 32	0	0	0	0	0	0	0	0	0	0	0
Week 33 to 40	0	0	0	0	0	0	0	0	0	0	0
Week 41 to 48	0	0	0	0	0	0	0	0	0	0	0

System Organ Class Preferred Term Time Period	Imeglimin N = 134	Imeglimin + SU N = 127	Imeglimin + GLIN N = 64	Imeglimin + BIG N = 64	Imeglimin + AGI N = 64	Imeglimin + TZD N = 65	Imeglimin + DPP4-I N = 63	Imeglimin + GLP1-RA N = 70	Imeglimin + SGLT2-I N = 63	Combination Total N = 580	Imeglimin Total N = 714
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Investigations (臨床検査)											
Lipase increased (リパーゼ増加)											
Week 1 to 4	0	0	0	0	0	0	0	0	0	0	0
Week 5 to 8	0	1 (0.8%)	0	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 9 to 16	0	1 (0.8%)	0	0	0	1 (1.5%)	2 (3.2%)	0	0	4 (0.7%)	4 (0.6%)
Week 17 to 24	1 (0.8%)	1 (0.8%)	0	0	0	0	0	0	0	1 (0.2%)	2 (0.3%)
Week 25 to 32	0	1 (0.8%)	0	0	1 (1.6%)	0	0	0	0	2 (0.4%)	2 (0.3%)
Week 33 to 40	0	0	0	0	0	1 (1.5%)	1 (1.6%)	0	0	2 (0.4%)	2 (0.3%)
Week 41 to 48	0	0	0	0	0	0	1 (1.7%)	0	0	1 (0.2%)	1 (0.1%)
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Surgical and medical procedures (外科および内科処置)											
Cataract operation (白内障手術)											
Week 1 to 4	0	0	0	0	0	0	0	0	0	0	0
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	0	0	1 (1.6%)	2 (3.1%)	1 (1.6%)	0	0	0	0	4 (0.7%)	4 (0.6%)
Week 17 to 24	1 (0.8%)	1 (0.8%)	0	0	0	0	0	0	0	1 (0.2%)	2 (0.3%)
Week 25 to 32	0	2 (1.6%)	0	0	0	0	0	0	0	2 (0.4%)	2 (0.3%)
Week 33 to 40	0	0	0	0	0	0	0	0	0	0	0
Week 41 to 48	0	0	0	0	0	0	0	0	0	0	0
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Cardiac disorders (心臓障害)											

System Organ Class Preferred Term Time Period	Imeglimin N = 134	Imeglimin + SU N = 127	Imeglimin + GLIN N = 64	Imeglimin + BIG N = 64	Imeglimin + AGI N = 64	Imeglimin + TZD N = 65	Imeglimin + DPP4-I N = 63	Imeglimin + GLP1-RA N = 70	Imeglimin + SGLT2-I N = 63	Combination Total N = 580	Imeglimin Total N = 714
Coronary artery stenosis (冠動脈狭窄)											
Week 1 to 4	0	0	0	0	0	0	0	0	0	0	0
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	0	0	0	0	0	0	0	0	0	0	0
Week 17 to 24	0	0	0	0	0	0	0	0	0	0	0
Week 25 to 32	0	0	0	0	0	0	0	0	0	0	0
Week 33 to 40	0	0	0	0	0	0	0	1 (1.4%)	0	1 (0.2%)	1 (0.1%)
Week 41 to 48	0	0	0	0	0	0	0	1 (1.4%)	0	1 (0.2%)	1 (0.1%)
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Palpitations (動悸)											
Week 1 to 4	0	0	0	0	0	0	0	0	0	0	0
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	0	0	0	1 (1.6%)	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 17 to 24	0	0	0	1 (1.6%)	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 25 to 32	0	0	0	0	0	0	0	0	0	0	0
Week 33 to 40	0	0	0	0	0	0	0	0	0	0	0
Week 41 to 48	0	0	0	0	0	0	0	0	0	0	0
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Sinus bradycardia (洞性徐脈)											
Week 1 to 4	0	0	0	0	0	0	0	0	0	0	0
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	0	0	0	0	0	0	0	0	0	0	0
Week 17 to 24	0	0	0	0	0	1 (1.5%)	0	0	0	1 (0.2%)	1 (0.1%)
Week 25 to 32	0	0	0	0	0	0	0	0	0	0	0
Week 33 to 40	0	0	0	0	0	0	0	0	0	0	0
Week 41 to 48	0	0	0	0	0	0	0	0	0	0	0
Week 49 or later	0	0	0	0	0	1 (1.5%)	0	0	0	1 (0.2%)	1 (0.1%)

System Organ Class Preferred Term Time Period	Imeglimin N = 134	Imeglimin + SU N = 127	Imeglimin + GLIN N = 64	Imeglimin + BIG N = 64	Imeglimin + AGI N = 64	Imeglimin + TZD N = 65	Imeglimin + DPP4-I N = 63	Imeglimin + GLP1-RA N = 70	Imeglimin + SGLT2-I N = 63	Combination Total N = 580	Imeglimin Total N = 714
General disorders and administration site conditions (一般・全身障害および投与部位の状態)											
Fatigue (疲労)											
Week 1 to 4	0	0	0	0	0	0	0	0	0	0	0
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	1 (0.8%)	0	0	0	0	0	0	0	0	0	1 (0.1%)
Week 17 to 24	0	0	0	0	0	0	1 (1.6%)	0	0	1 (0.2%)	1 (0.1%)
Week 25 to 32	0	0	1 (1.6%)	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 33 to 40	0	0	0	0	0	0	0	0	1 (1.6%)	1 (0.2%)	1 (0.1%)
Week 41 to 48	0	0	0	0	0	0	1 (1.7%)	0	0	1 (0.2%)	1 (0.1%)
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0
Ear and labyrinth disorders (耳および迷路障害)											
Vertigo (回転性めまい)											
Week 1 to 4	0	0	0	0	0	0	0	0	0	0	0
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	1 (0.8%)	0	0	2 (3.1%)	0	0	0	0	0	2 (0.3%)	3 (0.4%)
Week 17 to 24	0	0	0	0	0	0	0	0	0	0	0
Week 25 to 32	0	0	0	0	0	0	0	0	0	0	0
Week 33 to 40	0	0	0	0	0	0	0	0	0	0	0
Week 41 to 48	0	0	0	0	0	0	0	1 (1.4%)	0	1 (0.2%)	1 (0.1%)
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0

System Organ Class Preferred Term Time Period	Imeglimin N = 134	Imeglimin + SU N = 127	Imeglimin + GLIN N = 64	Imeglimin + BIG N = 64	Imeglimin + AGI N = 64	Imeglimin + TZD N = 65	Imeglimin + DPP4-I N = 63	Imeglimin + GLP1-RA N = 70	Imeglimin + SGLT2-I N = 63	Combination Total N = 580	Imeglimin Total N = 714
Reproductive system and breast disorders (生殖系および乳房障害)											
Benign prostatic hyperplasia (良性前立腺肥大症)											
Week 1 to 4	0	0	0	0	0	0	0	0	0	0	0
Week 5 to 8	0	0	0	0	0	0	0	0	0	0	0
Week 9 to 16	1 (0.8%)	0	0	0	0	0	0	0	0	0	1 (0.1%)
Week 17 to 24	0	0	1 (1.6%)	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Week 25 to 32	0	0	0	0	0	0	0	0	0	0	0
Week 33 to 40	0	0	0	0	0	0	0	0	0	0	0
Week 41 to 48	0	0	0	0	0	0	0	0	0	0	0
Week 49 or later	0	0	1 (1.7%)	0	0	0	0	0	0	1 (0.2%)	1 (0.1%)
Immune system disorders (免疫系障害)											
Allergy to arthropod sting (節足動物刺傷アレルギー)											
Week 1 to 4	0	0	0	0	0	0	0	0	0	0	0
Week 5 to 8	0	0	0	0	0	0	0	1 (1.4%)	0	1 (0.2%)	1 (0.1%)
Week 9 to 16	0	0	0	0	0	0	0	0	0	0	0
Week 17 to 24	0	0	0	0	0	0	0	0	0	0	0
Week 25 to 32	0	0	0	0	0	0	0	0	0	0	0
Week 33 to 40	0	0	0	0	0	0	0	1 (1.4%)	0	1 (0.2%)	1 (0.1%)
Week 41 to 48	0	0	0	0	0	0	0	0	0	0	0

System Organ Class Preferred Term Time Period	Imeglimin N = 134	Imeglimin + SU N = 127	Imeglimin + GLIN N = 64	Imeglimin + BIG N = 64	Imeglimin + AGI N = 64	Imeglimin + TZD N = 65	Imeglimin + DPP4-I N = 63	Imeglimin + GLP1-RA N = 70	Imeglimin + SGLT2-I N = 63	Combination Total N = 580	Imeglimin Total N = 714
Week 49 or later	0	0	0	0	0	0	0	0	0	0	0

- Abbreviations: AE, Adverse event; TEAE, Treatment Emergent AE; SU, Sulphonylurea; GLIN, Glinide; BIG, Biguanide; AGI, Alpha glucosidase inhibitor; TZD, Thiazolidinedione; DPP4-I, Dipeptidyl peptidase-4 inhibitor; GLP1-RA, Glucagon-like peptide 1 receptor agonist; SGLT2-I, Sodium glucose cotransporter 2 inhibitor
- "Imeglimin" in this table means "Imeglimin 1000 mg twice daily".
- "Combination Total" is the sum of the subjects excluding monotherapy "Imeglimin".
- "Imeglimin Total" is the sum of all subjects in Imeglimin treatment groups.
- All adverse events were coded using MedDRA dictionary version 20.1.
- Within each subject and each period, multiple reports of adverse events mapped to a common System Organ Class and Preferred Term are counted only once.
- Number of patients in each period is defined as that of patients whose study duration was equal to or greater than the initial day of the corresponding time period.
- Percentages are based on "Number of patients in each period".
- Time Period: Week 1 to 4 = Day 1 to 28, Week 5 to 8 = Day 29 to 56, Week 9 to 16 = Day 57 to 112, Week 17 to 24 = Day 113 to 168, Week 25 to 32 = Day 169 to 224, Week 33 to 40 = Day 225 to 280, Week 41 to 48 = Day 281 to 336, Week 49 or later = Day 337 or later.

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Table S-076 Summary of Treatment Emergent Adverse Events (Incidence >= 2%) by Timing of Initial Onset, System Organ Class and Preferred Term in 16-Week Double-blind Period in Combination with Insulin Therapy (PXL008-020; Safety Population)

System Organ Class Preferred Term Time Period	Placebo + Insulin N = 107	Imeglimin 1000 mg bid + Insulin N = 108
Number of patients in each period		
Week 1 to 4	107	108
Week 5 to 8	106	108
Week 9 to 12	106	108
Week 13 or later	105	108
Any TEAE		
Week 1 to 4	20 (18.7%)	25 (23.1%)
Week 5 to 8	13 (12.3%)	14 (13.0%)
Week 9 to 12	9 (8.5%)	10 (9.3%)
Week 13 or later	9 (8.6%)	8 (7.4%)
Metabolism and nutrition disorders (代謝および栄養障害)		
Hypoglycaemia (低血糖)		
Week 1 to 4	6 (5.6%)	12 (11.1%)
Week 5 to 8	3 (2.8%)	7 (6.5%)
Week 9 to 12	3 (2.8%)	3 (2.8%)
Week 13 or later	5 (4.8%)	1 (0.9%)
Hyperglycaemia (高血糖)		
Week 1 to 4	0	0
Week 5 to 8	1 (0.9%)	0
Week 9 to 12	1 (0.9%)	0
Week 13 or later	1 (1.0%)	0
Infections and infestations (感染症および寄生虫症)		
Nasopharyngitis (上咽頭炎)		
Week 1 to 4	3 (2.8%)	3 (2.8%)
Week 5 to 8	0	3 (2.8%)
Week 9 to 12	1 (0.9%)	4 (3.7%)
Week 13 or later	4 (3.8%)	6 (5.6%)
Bronchitis (気管支炎)		
Week 1 to 4	0	1 (0.9%)
Week 5 to 8	0	0
Week 9 to 12	0	2 (1.9%)
Week 13 or later	0	0
Gastrointestinal disorders (胃腸障害)		
Constipation (便秘)		
Week 1 to 4	1 (0.9%)	2 (1.9%)
Week 5 to 8	0	1 (0.9%)
Week 9 to 12	0	0
Week 13 or later	0	0

System Organ Class Preferred Term Time Period	Placebo + Insulin N = 107	Imeglimin 1000 mg bid + Insulin N = 108
General disorders and administration site conditions (一般・全身障害および投与部位の状態)		
Pyrexia (発熱)		
Week 1 to 4	0	0
Week 5 to 8	2 (1.9%)	1 (0.9%)
Week 9 to 12	1 (0.9%)	0
Week 13 or later	0	0
Nervous system disorders (神経系障害)		
Dizziness (浮動性めまい)		
Week 1 to 4	1 (0.9%)	0
Week 5 to 8	0	1 (0.9%)
Week 9 to 12	1 (0.9%)	0
Week 13 or later	1 (1.0%)	0

- Abbreviations: bid, Twice a day; AE, Adverse event; TEAE, Treatment Emergent AE
- All adverse events were coded using MedDRA dictionary version 20.1.
- Within each subject, multiple reports of adverse events mapped to a common System Organ Class and Preferred Term are counted only once.
- Number of patients in each period is defined as that of patients whose study duration was equal to or greater than the initial day of the corresponding time period.
- Percentages are based on "Number of patients in each period".
- Time Period: Week 1 to 4 = Day 1 to 28, Week 5 to 8 = Day 29 to 56, Week 9 to 12 = Day 57 to 84, Week 13 or later = Day 85 or later.

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Table S-077 Summary of Treatment Emergent Adverse Events (Incidence >= 2%) by Timing of Every Onset, System Organ Class and Preferred Term in 16-Week Double-blind Period in Combination with Insulin Therapy (PXL008-020; Safety Population)

System Organ Class Preferred Term Time Period	Placebo + Insulin N = 107	Imeglimin 1000 mg bid + Insulin N = 108
Number of patients in each period		
Week 1 to 4	107	108
Week 5 to 8	106	108
Week 9 to 12	106	108
Week 13 or later	105	108
Any TEAE		
Week 1 to 4	20 (18.7%)	25 (23.1%)
Week 5 to 8	15 (14.2%)	28 (25.9%)
Week 9 to 12	12 (11.3%)	26 (24.1%)
Week 13 or later	22 (21.0%)	24 (22.2%)
Metabolism and nutrition disorders (代謝および栄養障害)		
Hypoglycaemia (低血糖)		
Week 1 to 4	6 (5.6%)	12 (11.1%)
Week 5 to 8	5 (4.7%)	14 (13.0%)
Week 9 to 12	3 (2.8%)	13 (12.0%)
Week 13 or later	8 (7.6%)	9 (8.3%)
Hyperglycaemia (高血糖)		
Week 1 to 4	0	0
Week 5 to 8	1 (0.9%)	0
Week 9 to 12	1 (0.9%)	0
Week 13 or later	1 (1.0%)	0
Infections and infestations (感染症および寄生虫症)		
Nasopharyngitis (上咽頭炎)		
Week 1 to 4	3 (2.8%)	3 (2.8%)
Week 5 to 8	0	3 (2.8%)
Week 9 to 12	1 (0.9%)	4 (3.7%)
Week 13 or later	5 (4.8%)	6 (5.6%)
Bronchitis (気管支炎)		
Week 1 to 4	0	1 (0.9%)
Week 5 to 8	0	0
Week 9 to 12	0	2 (1.9%)
Week 13 or later	0	0
Gastrointestinal disorders (胃腸障害)		
Constipation (便秘)		
Week 1 to 4	1 (0.9%)	2 (1.9%)
Week 5 to 8	0	1 (0.9%)
Week 9 to 12	0	0
Week 13 or later	0	0

System Organ Class Preferred Term Time Period	Placebo + Insulin N = 107	Imeglimin 1000 mg bid + Insulin N = 108
General disorders and administration site conditions (一般・全身障害および投与部位の状態)		
Pyrexia (発熱)		
Week 1 to 4	0	0
Week 5 to 8	2 (1.9%)	1 (0.9%)
Week 9 to 12	1 (0.9%)	0
Week 13 or later	0	0
Nervous system disorders (神経系障害)		
Dizziness (浮動性めまい)		
Week 1 to 4	1 (0.9%)	0
Week 5 to 8	0	1 (0.9%)
Week 9 to 12	1 (0.9%)	0
Week 13 or later	1 (1.0%)	0

- Abbreviations: bid, Twice a day; AE, Adverse event; TEAE, Treatment Emergent AE
- All adverse events were coded using MedDRA dictionary version 20.1.
- Within each subject and each period, multiple reports of adverse events mapped to a common System Organ Class and Preferred Term are counted only once.
- Number of patients in each period is defined as that of patients whose study duration was equal to or greater than the initial day of the corresponding time period.
- Percentages are based on "Number of patients in each period".
- Time Period: Week 1 to 4 = Day 1 to 28, Week 5 to 8 = Day 29 to 56, Week 9 to 12 = Day 57 to 84, Week 13 or later = Day 85 or later.

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Table S-080 Summary of Treatment Emergent Adverse Events (Incidence >= 2%) by Timing of Initial Onset, System Organ Class and Preferred Term in 52-Week Long-term Period in Combination with Insulin Therapy (PXL008-020; Long-term Safety Population)

System Organ Class Preferred Term Time Period	Placebo/Imeglimin + Insulin N = 101	Imeglimin/Imeglimin + Insulin N = 108	Imeglimin + Insulin Total N = 209
Number of patients in each period			
Week 1 to 4	101	108	209
Week 5 to 8	101	108	209
Week 9 to 16	101	108	209
Week 17 to 24	99	108	207
Week 25 to 32	99	108	207
Week 33 to 40	98	108	206
Week 41 to 48	2	107	109
Week 49 or later	0	107	107
Any TEAE			
Week 1 to 4	19 (18.8%)	25 (23.1%)	44 (21.1%)
Week 5 to 8	14 (13.9%)	14 (13.0%)	28 (13.4%)
Week 9 to 16	19 (18.8%)	18 (16.7%)	37 (17.7%)
Week 17 to 24	13 (13.1%)	12 (11.1%)	25 (12.1%)
Week 25 to 32	8 (8.1%)	8 (7.4%)	16 (7.7%)
Week 33 to 40	4 (4.1%)	13 (12.0%)	17 (8.3%)
Week 41 to 48	0	2 (1.9%)	2 (1.8%)
Week 49 or later	.	0	0
Metabolism and nutrition disorders (代謝および栄養障害)			
Hypoglycaemia (低血糖)			
Week 1 to 4	7 (6.9%)	12 (11.1%)	19 (9.1%)
Week 5 to 8	7 (6.9%)	7 (6.5%)	14 (6.7%)
Week 9 to 16	9 (8.9%)	4 (3.7%)	13 (6.2%)
Week 17 to 24	6 (6.1%)	4 (3.7%)	10 (4.8%)
Week 25 to 32	3 (3.0%)	6 (5.6%)	9 (4.3%)
Week 33 to 40	4 (4.1%)	6 (5.6%)	10 (4.9%)
Week 41 to 48	0	0	0
Week 49 or later	.	0	0
Infections and infestations (感染症および寄生虫症)			
Nasopharyngitis (上咽頭炎)			
Week 1 to 4	3 (3.0%)	3 (2.8%)	6 (2.9%)
Week 5 to 8	1 (1.0%)	3 (2.8%)	4 (1.9%)
Week 9 to 16	3 (3.0%)	10 (9.3%)	13 (6.2%)
Week 17 to 24	3 (3.0%)	9 (8.3%)	12 (5.8%)
Week 25 to 32	2 (2.0%)	2 (1.9%)	4 (1.9%)
Week 33 to 40	4 (4.1%)	4 (3.7%)	8 (3.9%)
Week 41 to 48	0	4 (3.7%)	4 (3.7%)
Week 49 or later	.	1 (0.9%)	1 (0.9%)
Bronchitis (気管支炎)			

System Organ Class Preferred Term Time Period	Placebo/Imeglimin + Insulin N = 101	Imeglimin/Imeglimin + Insulin N = 108	Imeglimin + Insulin Total N = 209
Week 1 to 4	1 (1.0%)	1 (0.9%)	2 (1.0%)
Week 5 to 8	1 (1.0%)	0	1 (0.5%)
Week 9 to 16	0	2 (1.9%)	2 (1.0%)
Week 17 to 24	1 (1.0%)	0	1 (0.5%)
Week 25 to 32	1 (1.0%)	0	1 (0.5%)
Week 33 to 40	1 (1.0%)	1 (0.9%)	2 (1.0%)
Week 41 to 48	0	0	0
Week 49 or later	.	0	0
Influenza (インフルエンザ)			
Week 1 to 4	0	0	0
Week 5 to 8	1 (1.0%)	0	1 (0.5%)
Week 9 to 16	1 (1.0%)	0	1 (0.5%)
Week 17 to 24	2 (2.0%)	2 (1.9%)	4 (1.9%)
Week 25 to 32	0	2 (1.9%)	2 (1.0%)
Week 33 to 40	0	1 (0.9%)	1 (0.5%)
Week 41 to 48	0	0	0
Week 49 or later	.	0	0
Gastroenteritis (胃腸炎)			
Week 1 to 4	1 (1.0%)	0	1 (0.5%)
Week 5 to 8	1 (1.0%)	0	1 (0.5%)
Week 9 to 16	1 (1.0%)	0	1 (0.5%)
Week 17 to 24	0	0	0
Week 25 to 32	1 (1.0%)	1 (0.9%)	2 (1.0%)
Week 33 to 40	0	0	0
Week 41 to 48	0	0	0
Week 49 or later	.	0	0
Cystitis (膀胱炎)			
Week 1 to 4	0	0	0
Week 5 to 8	0	0	0
Week 9 to 16	0	0	0
Week 17 to 24	1 (1.0%)	0	1 (0.5%)
Week 25 to 32	0	1 (0.9%)	1 (0.5%)
Week 33 to 40	0	1 (0.9%)	1 (0.5%)
Week 41 to 48	0	0	0
Week 49 or later	.	1 (0.9%)	1 (0.9%)
Conjunctivitis (結膜炎)			
Week 1 to 4	0	0	0
Week 5 to 8	1 (1.0%)	0	1 (0.5%)
Week 9 to 16	0	0	0
Week 17 to 24	0	0	0
Week 25 to 32	0	0	0
Week 33 to 40	1 (1.0%)	0	1 (0.5%)
Week 41 to 48	0	0	0
Week 49 or later	.	0	0
Gastrointestinal disorders (胃腸障害)			
Constipation (便秘)			

System Organ Class Preferred Term Time Period	Placebo/Imeglimin + Insulin N = 101	Imeglimin/Imeglimin + Insulin N = 108	Imeglimin + Insulin Total N = 209
Week 1 to 4	0	2 (1.9%)	2 (1.0%)
Week 5 to 8	0	1 (0.9%)	1 (0.5%)
Week 9 to 16	0	0	0
Week 17 to 24	0	0	0
Week 25 to 32	0	1 (0.9%)	1 (0.5%)
Week 33 to 40	0	1 (0.9%)	1 (0.5%)
Week 41 to 48	0	1 (0.9%)	1 (0.9%)
Week 49 or later	.	0	0
Gastrooesophageal reflux disease (胃食道逆流性疾患)			
Week 1 to 4	1 (1.0%)	0	1 (0.5%)
Week 5 to 8	0	0	0
Week 9 to 16	1 (1.0%)	1 (0.9%)	2 (1.0%)
Week 17 to 24	0	0	0
Week 25 to 32	0	1 (0.9%)	1 (0.5%)
Week 33 to 40	0	0	0
Week 41 to 48	0	1 (0.9%)	1 (0.9%)
Week 49 or later	.	0	0
Nausea (悪心)			
Week 1 to 4	1 (1.0%)	1 (0.9%)	2 (1.0%)
Week 5 to 8	0	0	0
Week 9 to 16	0	1 (0.9%)	1 (0.5%)
Week 17 to 24	1 (1.0%)	0	1 (0.5%)
Week 25 to 32	0	1 (0.9%)	1 (0.5%)
Week 33 to 40	0	0	0
Week 41 to 48	0	0	0
Week 49 or later	.	0	0
Abdominal discomfort (腹部不快感)			
Week 1 to 4	0	1 (0.9%)	1 (0.5%)
Week 5 to 8	0	0	0
Week 9 to 16	0	0	0
Week 17 to 24	1 (1.0%)	1 (0.9%)	2 (1.0%)
Week 25 to 32	0	0	0
Week 33 to 40	0	1 (0.9%)	1 (0.5%)
Week 41 to 48	0	0	0
Week 49 or later	.	0	0
Diarrhoea (下痢)			
Week 1 to 4	1 (1.0%)	2 (1.9%)	3 (1.4%)
Week 5 to 8	1 (1.0%)	0	1 (0.5%)
Week 9 to 16	0	0	0
Week 17 to 24	0	0	0
Week 25 to 32	0	0	0
Week 33 to 40	0	0	0
Week 41 to 48	0	0	0
Week 49 or later	.	0	0
Toothache (歯痛)			
Week 1 to 4	1 (1.0%)	0	1 (0.5%)
Week 5 to 8	0	0	0

System Organ Class Preferred Term Time Period	Placebo/Imeglimin + Insulin N = 101	Imeglimin/Imeglimin + Insulin N = 108	Imeglimin + Insulin Total N = 209
Week 9 to 16	1 (1.0%)	1 (0.9%)	2 (1.0%)
Week 17 to 24	0	0	0
Week 25 to 32	0	0	0
Week 33 to 40	0	0	0
Week 41 to 48	0	0	0
Week 49 or later	.	0	0
Chronic gastritis (慢性胃炎)			
Week 1 to 4	1 (1.0%)	0	1 (0.5%)
Week 5 to 8	0	0	0
Week 9 to 16	0	0	0
Week 17 to 24	0	0	0
Week 25 to 32	1 (1.0%)	0	1 (0.5%)
Week 33 to 40	0	0	0
Week 41 to 48	0	0	0
Week 49 or later	.	0	0
Musculoskeletal and connective tissue disorders (筋骨格系および結合組織障害)			
Back pain (背部痛)			
Week 1 to 4	0	0	0
Week 5 to 8	0	0	0
Week 9 to 16	0	0	0
Week 17 to 24	1 (1.0%)	1 (0.9%)	2 (1.0%)
Week 25 to 32	0	0	0
Week 33 to 40	0	1 (0.9%)	1 (0.5%)
Week 41 to 48	0	3 (2.8%)	3 (2.8%)
Week 49 or later	.	1 (0.9%)	1 (0.9%)
Muscle spasms (筋痙縮)			
Week 1 to 4	0	1 (0.9%)	1 (0.5%)
Week 5 to 8	0	0	0
Week 9 to 16	0	1 (0.9%)	1 (0.5%)
Week 17 to 24	0	0	0
Week 25 to 32	1 (1.0%)	1 (0.9%)	2 (1.0%)
Week 33 to 40	0	0	0
Week 41 to 48	0	1 (0.9%)	1 (0.9%)
Week 49 or later	.	0	0
Arthralgia (関節痛)			
Week 1 to 4	0	0	0
Week 5 to 8	0	1 (0.9%)	1 (0.5%)
Week 9 to 16	1 (1.0%)	1 (0.9%)	2 (1.0%)
Week 17 to 24	0	0	0
Week 25 to 32	0	1 (0.9%)	1 (0.5%)
Week 33 to 40	0	0	0
Week 41 to 48	0	0	0
Week 49 or later	.	0	0
Spinal osteoarthritis (変形性脊椎症)			

System Organ Class Preferred Term Time Period	Placebo/Imeglimin + Insulin N = 101	Imeglimin/Imeglimin + Insulin N = 108	Imeglimin + Insulin Total N = 209
Week 1 to 4	0	0	0
Week 5 to 8	0	0	0
Week 9 to 16	0	1 (0.9%)	1 (0.5%)
Week 17 to 24	0	0	0
Week 25 to 32	0	1 (0.9%)	1 (0.5%)
Week 33 to 40	0	1 (0.9%)	1 (0.5%)
Week 41 to 48	0	0	0
Week 49 or later	.	1 (0.9%)	1 (0.9%)
Vascular disorders (血管障害)			
Hypertension (高血圧)			
Week 1 to 4	0	0	0
Week 5 to 8	0	0	0
Week 9 to 16	1 (1.0%)	0	1 (0.5%)
Week 17 to 24	0	4 (3.7%)	4 (1.9%)
Week 25 to 32	0	1 (0.9%)	1 (0.5%)
Week 33 to 40	1 (1.0%)	0	1 (0.5%)
Week 41 to 48	0	0	0
Week 49 or later	.	0	0
Nervous system disorders (神経系障害)			
Headache (頭痛)			
Week 1 to 4	0	0	0
Week 5 to 8	1 (1.0%)	0	1 (0.5%)
Week 9 to 16	0	0	0
Week 17 to 24	1 (1.0%)	0	1 (0.5%)
Week 25 to 32	0	0	0
Week 33 to 40	1 (1.0%)	1 (0.9%)	2 (1.0%)
Week 41 to 48	0	2 (1.9%)	2 (1.8%)
Week 49 or later	.	0	0
Respiratory, thoracic and mediastinal disorders (呼吸器、胸郭および縦隔障害)			
Upper respiratory tract inflammation (上気道の炎症)			
Week 1 to 4	1 (1.0%)	0	1 (0.5%)
Week 5 to 8	0	0	0
Week 9 to 16	0	0	0
Week 17 to 24	2 (2.0%)	0	2 (1.0%)
Week 25 to 32	0	0	0
Week 33 to 40	0	1 (0.9%)	1 (0.5%)
Week 41 to 48	0	0	0
Week 49 or later	.	0	0
Sputum increased (喀痰増加)			
Week 1 to 4	0	0	0
Week 5 to 8	1 (1.0%)	0	1 (0.5%)
Week 9 to 16	1 (1.0%)	0	1 (0.5%)

System Organ Class Preferred Term Time Period	Placebo/Imeglimin + Insulin N = 101	Imeglimin/Imeglimin + Insulin N = 108	Imeglimin + Insulin Total N = 209
Week 17 to 24	0	0	0
Week 25 to 32	0	0	0
Week 33 to 40	0	0	0
Week 41 to 48	0	0	0
Week 49 or later	.	0	0
Immune system disorders (免疫系障害)			
Seasonal allergy (季節性アレルギー)			
Week 1 to 4	0	0	0
Week 5 to 8	0	0	0
Week 9 to 16	1 (1.0%)	0	1 (0.5%)
Week 17 to 24	0	0	0
Week 25 to 32	0	1 (0.9%)	1 (0.5%)
Week 33 to 40	0	1 (0.9%)	1 (0.5%)
Week 41 to 48	0	2 (1.9%)	2 (1.8%)
Week 49 or later	.	0	0
General disorders and administration site conditions (一般・全身障害および投与部位の状態)			
Pyrexia (発熱)			
Week 1 to 4	1 (1.0%)	0	1 (0.5%)
Week 5 to 8	0	1 (0.9%)	1 (0.5%)
Week 9 to 16	0	0	0
Week 17 to 24	0	0	0
Week 25 to 32	1 (1.0%)	0	1 (0.5%)
Week 33 to 40	0	1 (0.9%)	1 (0.5%)
Week 41 to 48	0	0	0
Week 49 or later	.	0	0
Eye disorders (眼障害)			
Diabetic retinopathy (糖尿病網膜症)			
Week 1 to 4	0	0	0
Week 5 to 8	0	0	0
Week 9 to 16	0	0	0
Week 17 to 24	0	1 (0.9%)	1 (0.5%)
Week 25 to 32	2 (2.0%)	0	2 (1.0%)
Week 33 to 40	0	0	0
Week 41 to 48	0	0	0
Week 49 or later	.	0	0
Injury, poisoning and procedural complications (傷害、中毒および処置合併症)			
Contusion (挫傷)			
Week 1 to 4	0	0	0
Week 5 to 8	0	0	0

System Organ Class Preferred Term Time Period	Placebo/Imeglimin + Insulin N = 101	Imeglimin/Imeglimin + Insulin N = 108	Imeglimin + Insulin Total N = 209
Week 9 to 16	0	0	0
Week 17 to 24	0	1 (0.9%)	1 (0.5%)
Week 25 to 32	0	1 (0.9%)	1 (0.5%)
Week 33 to 40	0	1 (0.9%)	1 (0.5%)
Week 41 to 48	0	0	0
Week 49 or later	.	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps) (良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）)			
Papillary thyroid cancer (乳頭様甲状腺癌)			
Week 1 to 4	0	0	0
Week 5 to 8	0	0	0
Week 9 to 16	1 (1.0%)	0	1 (0.5%)
Week 17 to 24	1 (1.0%)	0	1 (0.5%)
Week 25 to 32	0	0	0
Week 33 to 40	0	0	0
Week 41 to 48	0	0	0
Week 49 or later	.	0	0

- Abbreviations: AE, Adverse event; TEAE, Treatment Emergent AE
- All adverse events were coded using MedDRA dictionary version 20.1.
- "Imeglimin" in this table means "Imeglimin 1000 mg twice daily".
- The Long-term Safety Population excludes data during administration of placebo in the double-blind period.
- "Imeglimin + Insulin Total" is the sum of subjects in the placebo group in the open-label period and Imeglimin group in the double-blind and open-label periods.
- Within each subject, multiple reports of adverse events mapped to a common System Organ Class and Preferred Term are counted only once.
- Number of patients in each period is defined as that of patients whose study duration was equal to or greater than the initial day of the corresponding time period.
- Percentages are based on "Number of patients in each period".
- Onset day for Placebo/Imeglimin + Insulin group was relative to the day of first dose of study treatment in the open-label period.
- Time Period: Week 1 to 4 = Day 1 to 28, Week 5 to 8 = Day 29 to 56, Week 9 to 16 = Day 57 to 112, Week 17 to 24 = Day 113 to 168, Week 25 to 32 = Day 169 to 224, Week 33 to 40 = Day 225 to 280, Week 41 to 48 = Day 281 to 336, Week 49 or later = Day 337 or later.

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Table S-081 Summary of Treatment Emergent Adverse Events (Incidence >= 2%) by Timing of Every Onset, System Organ Class and Preferred Term in 52-Week Long-term Period in Combination with Insulin Therapy (PXL008-020; Long-term Safety Population)

System Organ Class Preferred Term Time Period	Placebo/Imeglimin + Insulin N = 101	Imeglimin/Imeglimin + Insulin N = 108	Imeglimin + Insulin Total N = 209
Number of patients in each period			
Week 1 to 4	101	108	209
Week 5 to 8	101	108	209
Week 9 to 16	101	108	209
Week 17 to 24	99	108	207
Week 25 to 32	99	108	207
Week 33 to 40	98	108	206
Week 41 to 48	2	107	109
Week 49 or later	0	107	107
Any TEAE			
Week 1 to 4	19 (18.8%)	25 (23.1%)	44 (21.1%)
Week 5 to 8	24 (23.8%)	28 (25.9%)	52 (24.9%)
Week 9 to 16	35 (34.7%)	40 (37.0%)	75 (35.9%)
Week 17 to 24	39 (39.4%)	48 (44.4%)	87 (42.0%)
Week 25 to 32	30 (30.3%)	38 (35.2%)	68 (32.9%)
Week 33 to 40	18 (18.4%)	46 (42.6%)	64 (31.1%)
Week 41 to 48	0	43 (40.2%)	43 (39.4%)
Week 49 or later	.	29 (27.1%)	29 (27.1%)
Metabolism and nutrition disorders (代謝および栄養障害)			
Hypoglycaemia (低血糖)			
Week 1 to 4	7 (6.9%)	12 (11.1%)	19 (9.1%)
Week 5 to 8	11 (10.9%)	14 (13.0%)	25 (12.0%)
Week 9 to 16	17 (16.8%)	17 (15.7%)	34 (16.3%)
Week 17 to 24	17 (17.2%)	20 (18.5%)	37 (17.9%)
Week 25 to 32	13 (13.1%)	20 (18.5%)	33 (15.9%)
Week 33 to 40	10 (10.2%)	22 (20.4%)	32 (15.5%)
Week 41 to 48	0	18 (16.8%)	18 (16.5%)
Week 49 or later	.	18 (16.8%)	18 (16.8%)
Infections and infestations (感染症および寄生虫症)			
Nasopharyngitis (上咽頭炎)			
Week 1 to 4	3 (3.0%)	3 (2.8%)	6 (2.9%)
Week 5 to 8	2 (2.0%)	3 (2.8%)	5 (2.4%)
Week 9 to 16	3 (3.0%)	10 (9.3%)	13 (6.2%)
Week 17 to 24	6 (6.1%)	11 (10.2%)	17 (8.2%)
Week 25 to 32	3 (3.0%)	3 (2.8%)	6 (2.9%)
Week 33 to 40	5 (5.1%)	8 (7.4%)	13 (6.3%)
Week 41 to 48	0	5 (4.7%)	5 (4.6%)
Week 49 or later	.	3 (2.8%)	3 (2.8%)
Bronchitis (気管支炎)			

System Organ Class Preferred Term Time Period	Placebo/Imeglimin + Insulin N = 101	Imeglimin/Imeglimin + Insulin N = 108	Imeglimin + Insulin Total N = 209
Week 1 to 4	1 (1.0%)	1 (0.9%)	2 (1.0%)
Week 5 to 8	1 (1.0%)	0	1 (0.5%)
Week 9 to 16	0	2 (1.9%)	2 (1.0%)
Week 17 to 24	1 (1.0%)	0	1 (0.5%)
Week 25 to 32	2 (2.0%)	0	2 (1.0%)
Week 33 to 40	1 (1.0%)	1 (0.9%)	2 (1.0%)
Week 41 to 48	0	0	0
Week 49 or later	.	1 (0.9%)	1 (0.9%)
Influenza (インフルエンザ)			
Week 1 to 4	0	0	0
Week 5 to 8	1 (1.0%)	0	1 (0.5%)
Week 9 to 16	1 (1.0%)	0	1 (0.5%)
Week 17 to 24	2 (2.0%)	2 (1.9%)	4 (1.9%)
Week 25 to 32	0	2 (1.9%)	2 (1.0%)
Week 33 to 40	0	1 (0.9%)	1 (0.5%)
Week 41 to 48	0	0	0
Week 49 or later	.	0	0
Gastroenteritis (胃腸炎)			
Week 1 to 4	1 (1.0%)	0	1 (0.5%)
Week 5 to 8	1 (1.0%)	0	1 (0.5%)
Week 9 to 16	1 (1.0%)	0	1 (0.5%)
Week 17 to 24	0	0	0
Week 25 to 32	1 (1.0%)	1 (0.9%)	2 (1.0%)
Week 33 to 40	0	0	0
Week 41 to 48	0	0	0
Week 49 or later	.	0	0
Cystitis (膀胱炎)			
Week 1 to 4	0	0	0
Week 5 to 8	0	0	0
Week 9 to 16	0	0	0
Week 17 to 24	1 (1.0%)	0	1 (0.5%)
Week 25 to 32	0	1 (0.9%)	1 (0.5%)
Week 33 to 40	0	1 (0.9%)	1 (0.5%)
Week 41 to 48	0	0	0
Week 49 or later	.	1 (0.9%)	1 (0.9%)
Conjunctivitis (結膜炎)			
Week 1 to 4	0	0	0
Week 5 to 8	1 (1.0%)	0	1 (0.5%)
Week 9 to 16	0	0	0
Week 17 to 24	0	0	0
Week 25 to 32	0	0	0
Week 33 to 40	1 (1.0%)	0	1 (0.5%)
Week 41 to 48	0	0	0
Week 49 or later	.	0	0
Gastrointestinal disorders (胃腸障害)			
Constipation (便秘)			

System Organ Class Preferred Term Time Period	Placebo/Imeglimin + Insulin N = 101	Imeglimin/Imeglimin + Insulin N = 108	Imeglimin + Insulin Total N = 209
Week 1 to 4	0	2 (1.9%)	2 (1.0%)
Week 5 to 8	0	1 (0.9%)	1 (0.5%)
Week 9 to 16	0	0	0
Week 17 to 24	0	0	0
Week 25 to 32	0	1 (0.9%)	1 (0.5%)
Week 33 to 40	0	1 (0.9%)	1 (0.5%)
Week 41 to 48	0	2 (1.9%)	2 (1.8%)
Week 49 or later	.	0	0
Gastrooesophageal reflux disease (胃食道逆流性疾患)			
Week 1 to 4	1 (1.0%)	0	1 (0.5%)
Week 5 to 8	0	0	0
Week 9 to 16	1 (1.0%)	1 (0.9%)	2 (1.0%)
Week 17 to 24	0	0	0
Week 25 to 32	0	1 (0.9%)	1 (0.5%)
Week 33 to 40	0	0	0
Week 41 to 48	0	1 (0.9%)	1 (0.9%)
Week 49 or later	.	0	0
Nausea (悪心)			
Week 1 to 4	1 (1.0%)	1 (0.9%)	2 (1.0%)
Week 5 to 8	0	0	0
Week 9 to 16	0	1 (0.9%)	1 (0.5%)
Week 17 to 24	1 (1.0%)	0	1 (0.5%)
Week 25 to 32	0	1 (0.9%)	1 (0.5%)
Week 33 to 40	0	1 (0.9%)	1 (0.5%)
Week 41 to 48	0	0	0
Week 49 or later	.	0	0
Abdominal discomfort (腹部不快感)			
Week 1 to 4	0	1 (0.9%)	1 (0.5%)
Week 5 to 8	0	0	0
Week 9 to 16	0	0	0
Week 17 to 24	1 (1.0%)	1 (0.9%)	2 (1.0%)
Week 25 to 32	0	0	0
Week 33 to 40	0	1 (0.9%)	1 (0.5%)
Week 41 to 48	0	0	0
Week 49 or later	.	0	0
Diarrhoea (下痢)			
Week 1 to 4	1 (1.0%)	2 (1.9%)	3 (1.4%)
Week 5 to 8	2 (2.0%)	0	2 (1.0%)
Week 9 to 16	0	0	0
Week 17 to 24	0	0	0
Week 25 to 32	0	0	0
Week 33 to 40	0	0	0
Week 41 to 48	0	0	0
Week 49 or later	.	0	0
Toothache (歯痛)			
Week 1 to 4	1 (1.0%)	0	1 (0.5%)
Week 5 to 8	0	0	0

System Organ Class Preferred Term Time Period	Placebo/Imeglimin + Insulin N = 101	Imeglimin/Imeglimin + Insulin N = 108	Imeglimin + Insulin Total N = 209
Week 9 to 16	1 (1.0%)	1 (0.9%)	2 (1.0%)
Week 17 to 24	0	0	0
Week 25 to 32	0	0	0
Week 33 to 40	0	0	0
Week 41 to 48	0	0	0
Week 49 or later	.	0	0
Chronic gastritis (慢性胃炎)			
Week 1 to 4	1 (1.0%)	0	1 (0.5%)
Week 5 to 8	0	0	0
Week 9 to 16	0	0	0
Week 17 to 24	0	0	0
Week 25 to 32	1 (1.0%)	0	1 (0.5%)
Week 33 to 40	0	0	0
Week 41 to 48	0	0	0
Week 49 or later	.	0	0
Musculoskeletal and connective tissue disorders (筋骨格系および結合組織障害)			
Back pain (背部痛)			
Week 1 to 4	0	0	0
Week 5 to 8	0	0	0
Week 9 to 16	0	0	0
Week 17 to 24	1 (1.0%)	1 (0.9%)	2 (1.0%)
Week 25 to 32	0	0	0
Week 33 to 40	0	1 (0.9%)	1 (0.5%)
Week 41 to 48	0	4 (3.7%)	4 (3.7%)
Week 49 or later	.	1 (0.9%)	1 (0.9%)
Muscle spasms (筋痙縮)			
Week 1 to 4	0	1 (0.9%)	1 (0.5%)
Week 5 to 8	0	0	0
Week 9 to 16	0	1 (0.9%)	1 (0.5%)
Week 17 to 24	0	0	0
Week 25 to 32	1 (1.0%)	1 (0.9%)	2 (1.0%)
Week 33 to 40	0	0	0
Week 41 to 48	0	1 (0.9%)	1 (0.9%)
Week 49 or later	.	0	0
Arthralgia (関節痛)			
Week 1 to 4	0	0	0
Week 5 to 8	0	1 (0.9%)	1 (0.5%)
Week 9 to 16	1 (1.0%)	1 (0.9%)	2 (1.0%)
Week 17 to 24	0	0	0
Week 25 to 32	0	1 (0.9%)	1 (0.5%)
Week 33 to 40	0	1 (0.9%)	1 (0.5%)
Week 41 to 48	0	0	0
Week 49 or later	.	0	0
Spinal osteoarthritis (変形性脊椎症)			

System Organ Class Preferred Term Time Period	Placebo/Imeglimin + Insulin N = 101	Imeglimin/Imeglimin + Insulin N = 108	Imeglimin + Insulin Total N = 209
Week 1 to 4	0	0	0
Week 5 to 8	0	0	0
Week 9 to 16	0	1 (0.9%)	1 (0.5%)
Week 17 to 24	0	0	0
Week 25 to 32	0	1 (0.9%)	1 (0.5%)
Week 33 to 40	0	1 (0.9%)	1 (0.5%)
Week 41 to 48	0	0	0
Week 49 or later	.	1 (0.9%)	1 (0.9%)
Vascular disorders (血管障害)			
Hypertension (高血圧)			
Week 1 to 4	0	0	0
Week 5 to 8	0	0	0
Week 9 to 16	1 (1.0%)	0	1 (0.5%)
Week 17 to 24	0	4 (3.7%)	4 (1.9%)
Week 25 to 32	0	1 (0.9%)	1 (0.5%)
Week 33 to 40	1 (1.0%)	0	1 (0.5%)
Week 41 to 48	0	0	0
Week 49 or later	.	0	0
Nervous system disorders (神経系障害)			
Headache (頭痛)			
Week 1 to 4	0	0	0
Week 5 to 8	1 (1.0%)	0	1 (0.5%)
Week 9 to 16	0	0	0
Week 17 to 24	1 (1.0%)	0	1 (0.5%)
Week 25 to 32	0	0	0
Week 33 to 40	1 (1.0%)	1 (0.9%)	2 (1.0%)
Week 41 to 48	0	2 (1.9%)	2 (1.8%)
Week 49 or later	.	0	0
Respiratory, thoracic and mediastinal disorders (呼吸器、胸郭および縦隔障害)			
Upper respiratory tract inflammation (上気道の炎症)			
Week 1 to 4	1 (1.0%)	0	1 (0.5%)
Week 5 to 8	0	0	0
Week 9 to 16	0	0	0
Week 17 to 24	2 (2.0%)	0	2 (1.0%)
Week 25 to 32	0	0	0
Week 33 to 40	0	1 (0.9%)	1 (0.5%)
Week 41 to 48	0	0	0
Week 49 or later	.	0	0
Sputum increased (喀痰増加)			
Week 1 to 4	0	0	0
Week 5 to 8	1 (1.0%)	0	1 (0.5%)
Week 9 to 16	1 (1.0%)	0	1 (0.5%)

System Organ Class Preferred Term Time Period	Placebo/Imeglimin + Insulin N = 101	Imeglimin/Imeglimin + Insulin N = 108	Imeglimin + Insulin Total N = 209
Week 17 to 24	0	0	0
Week 25 to 32	0	0	0
Week 33 to 40	0	0	0
Week 41 to 48	0	0	0
Week 49 or later	.	0	0
Immune system disorders (免疫系障害)			
Seasonal allergy (季節性アレルギー)			
Week 1 to 4	0	0	0
Week 5 to 8	0	0	0
Week 9 to 16	1 (1.0%)	0	1 (0.5%)
Week 17 to 24	0	0	0
Week 25 to 32	0	1 (0.9%)	1 (0.5%)
Week 33 to 40	0	1 (0.9%)	1 (0.5%)
Week 41 to 48	0	2 (1.9%)	2 (1.8%)
Week 49 or later	.	0	0
General disorders and administration site conditions (一般・全身障害および投与部位の状態)			
Pyrexia (発熱)			
Week 1 to 4	1 (1.0%)	0	1 (0.5%)
Week 5 to 8	0	1 (0.9%)	1 (0.5%)
Week 9 to 16	0	0	0
Week 17 to 24	0	0	0
Week 25 to 32	1 (1.0%)	0	1 (0.5%)
Week 33 to 40	0	1 (0.9%)	1 (0.5%)
Week 41 to 48	0	0	0
Week 49 or later	.	0	0
Eye disorders (眼障害)			
Diabetic retinopathy (糖尿病網膜症)			
Week 1 to 4	0	0	0
Week 5 to 8	0	0	0
Week 9 to 16	0	0	0
Week 17 to 24	0	1 (0.9%)	1 (0.5%)
Week 25 to 32	2 (2.0%)	0	2 (1.0%)
Week 33 to 40	0	0	0
Week 41 to 48	0	0	0
Week 49 or later	.	0	0
Injury, poisoning and procedural complications (傷害、中毒および処置合併症)			
Contusion (挫傷)			
Week 1 to 4	0	0	0
Week 5 to 8	0	0	0

System Organ Class Preferred Term Time Period	Placebo/Imeglimin + Insulin N = 101	Imeglimin/Imeglimin + Insulin N = 108	Imeglimin + Insulin Total N = 209
Week 9 to 16	0	0	0
Week 17 to 24	0	1 (0.9%)	1 (0.5%)
Week 25 to 32	0	1 (0.9%)	1 (0.5%)
Week 33 to 40	0	1 (0.9%)	1 (0.5%)
Week 41 to 48	0	0	0
Week 49 or later	.	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps) (良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）)			
Papillary thyroid cancer (乳頭様甲状腺癌)			
Week 1 to 4	0	0	0
Week 5 to 8	0	0	0
Week 9 to 16	1 (1.0%)	0	1 (0.5%)
Week 17 to 24	1 (1.0%)	0	1 (0.5%)
Week 25 to 32	0	0	0
Week 33 to 40	0	0	0
Week 41 to 48	0	0	0
Week 49 or later	.	0	0

- Abbreviations: AE, Adverse event; TEAE, Treatment Emergent AE
- All adverse events were coded using MedDRA dictionary version 20.1.
- "Imeglimin" in this table means "Imeglimin 1000 mg twice daily".
- The Long-term Safety Population excludes data during administration of placebo in the double-blind period.
- "Imeglimin + Insulin Total" is the sum of subjects in the placebo group in the open-label period and Imeglimin group in the double-blind and open-label periods.
- Within each subject and each period, multiple reports of adverse events mapped to a common System Organ Class and Preferred Term are counted only once.
- Number of patients in each period is defined as that of patients whose study duration was equal to or greater than the initial day of the corresponding time period.
- Percentages are based on "Number of patients in each period".
- Onset day for Placebo/Imeglimin + Insulin group was relative to the day of first dose of study treatment in the open-label period.
- Time Period: Week 1 to 4 = Day 1 to 28, Week 5 to 8 = Day 29 to 56, Week 9 to 16 = Day 57 to 112, Week 17 to 24 = Day 113 to 168, Week 25 to 32 = Day 169 to 224, Week 33 to 40 = Day 225 to 280, Week 41 to 48 = Day 281 to 336, Week 49 or later = Day 337 or later.

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Table S-092 Summary of Markedly Abnormal Post-Baseline Laboratory Values in 24-Week Double-blind Period with Monotherapy (PXL008-014, PXL008-018; Safety Population)

Parameter Criteria	Placebo N = 182 n/m (%)	Imeglimin 500 mg bid N = 75 n/m (%)	Imeglimin 1000 mg bid N = 180 n/m (%)	Imeglimin 1500 mg bid N = 75 n/m (%)	Imeglimin Total N = 330 n/m (%)
Activated Partial Thromboplastin Time (sec)					
> 1.5 x ULN	0/167	0/71	0/172	0/66	0/309
Alanine Aminotransferase (U/L)					
>= 3 x ULN	1/181 (0.6%)	1/75 (1.3%)	0/180	1/75 (1.3%)	2/330 (0.6%)
Albumin (g/L)					
<= 25 g/L	0/181	0/75	0/180	0/75	0/330
Alkaline Phosphatase (U/L)					
>= 1.5 x ULN	0/181	0/75	1/180 (0.6%)	0/75	1/330 (0.3%)
Aspartate Aminotransferase (U/L)					
>= 3 x ULN	3/181 (1.7%)	0/75	0/180	0/75	0/330
Basophils (10^9/L)					
> 1.6 x 10^9/L	0/181	0/75	0/180	0/75	0/330
Basophils/Leukocytes (%)					
>= 10%	0/181	0/75	0/180	0/75	0/330
Bilirubin (umol/L)					
>= 34.2 umol/L or > 2 x ULN	2/181 (1.1%)	1/75 (1.3%)	3/180 (1.7%)	0/75	4/330 (1.2%)
Calcium (mmol/L)					
< 1.75 mmol/L	0/181	0/75	0/180	0/75	0/330
>= 3.1 mmol/L	0/181	0/75	0/180	0/75	0/330
Chloride (mmol/L)					
<= 90 mmol/L	0/181	0/75	0/180	1/75 (1.3%)	1/330 (0.3%)
>= 118 mmol/L	0/181	0/75	0/180	0/75	0/330
Creatine Kinase (U/L)					
> 2.5 x ULN	3/181 (1.7%)	2/75 (2.7%)	3/180 (1.7%)	2/75 (2.7%)	7/330 (2.1%)
Creatinine (umol/L)					
>= 177 umol/L	0/181	0/75	0/180	0/75	0/330
Eosinophils (10^9/L)					
> 1.6 x 10^9/L	0/181	0/75	1/180 (0.6%)	0/75	1/330 (0.3%)
Eosinophils/Leukocytes (%)					
>= 10%	8/181 (4.4%)	9/75 (12.0%)	11/180 (6.1%)	8/75 (10.7%)	28/330 (8.5%)
Erythrocytes (10^12/L)					

Parameter Criteria	Placebo N = 182 n/m (%)	Imeglimin 500 mg bid N = 75 n/m (%)	Imeglimin 1000 mg bid N = 180 n/m (%)	Imeglimin 1500 mg bid N = 75 n/m (%)	Imeglimin Total N = 330 n/m (%)
<= 3.5 x 10^12/L	2/181 (1.1%)	0/75	5/180 (2.8%)	2/75 (2.7%)	7/330 (2.1%)
>= 6.4 x 10^12/L	0/181	0/75	0/180	0/75	0/330
Gamma Glutamyl Transferase (U/L)					
>= 2.5 x ULN	9/181 (5.0%)	8/75 (10.7%)	5/180 (2.8%)	6/75 (8.0%)	19/330 (5.8%)
Hematocrit (fraction of 1)					
<= 0.37 for male, <= 0.32 for female	11/181 (6.1%)	1/75 (1.3%)	14/180 (7.8%)	4/75 (5.3%)	19/330 (5.8%)
>= 0.60 for male, >= 0.54 for female	0/181	0/75	0/180	0/75	0/330
Hemoglobin (g/L)					
<= 115 g/L for male, <= 95 g/L for female	1/181 (0.6%)	1/75 (1.3%)	5/180 (2.8%)	2/75 (2.7%)	8/330 (2.4%)
>= 190 g/L for male, >= 175 g/L for female	1/181 (0.6%)	0/75	0/180	0/75	0/330
Lactic Acid (mmol/L)					
> 5 mmol/L	0/176	0/75	1/178 (0.6%)	1/75 (1.3%)	2/328 (0.6%)
Leukocytes (10^9/L)					
<= 2.8 x 10^9/L	9/181 (5.0%)	2/75 (2.7%)	6/180 (3.3%)	3/75 (4.0%)	11/330 (3.3%)
>= 16 x 10^9/L	0/181	0/75	0/180	0/75	0/330
Lipase (U/L)					
>= 3 x ULN	1/181 (0.6%)	0/75	2/180 (1.1%)	0/75	2/330 (0.6%)
Lymphocytes (10^9/L)					
> 12 x 10^9/L	0/181	0/75	0/180	0/75	0/330
Lymphocytes/Leukocytes (%)					
>= 75%	0/181	0/75	1/180 (0.6%)	0/75	1/330 (0.3%)
Monocytes (10^9/L)					
> 2.5 x 10^9/L	0/181	0/75	0/180	0/75	0/330
Monocytes/Leukocytes (%)					
>= 15%	0/181	4/75 (5.3%)	4/180 (2.2%)	5/75 (6.7%)	13/330 (3.9%)
Neutrophils (10^9/L)					
< 0.5 x 10^9/L	1/181 (0.6%)	1/75 (1.3%)	2/180 (1.1%)	1/75 (1.3%)	4/330 (1.2%)
> 13.5 x 10^9/L	0/181	0/75	0/180	0/75	0/330
Neutrophils/Leukocytes (%)					
<= 15%	0/181	0/75	3/180 (1.7%)	1/75 (1.3%)	4/330 (1.2%)
> 85%	2/181 (1.1%)	0/75	1/180 (0.6%)	0/75	1/330 (0.3%)
Phosphate (mmol/L)					

Parameter Criteria	Placebo N = 182 n/m (%)	Imeglimin 500 mg bid N = 75 n/m (%)	Imeglimin 1000 mg bid N = 180 n/m (%)	Imeglimin 1500 mg bid N = 75 n/m (%)	Imeglimin Total N = 330 n/m (%)
< 0.65 mmol/L	0/181	0/75	0/180	0/75	0/330
> 1.65 mmol/L	0/181	2/75 (2.7%)	2/180 (1.1%)	1/75 (1.3%)	5/330 (1.5%)
Platelets (10^9/L)					
<= 75 x 10^9/L	0/181	0/75	0/180	1/75 (1.3%)	1/330 (0.3%)
>= 700 x 10^9/L	0/181	0/75	0/180	0/75	0/330
Potassium (mmol/L)					
< 3 mmol/L	0/181	0/75	0/180	0/75	0/330
> 5.5 mmol/L	1/181 (0.6%)	3/75 (4.0%)	1/180 (0.6%)	1/75 (1.3%)	5/330 (1.5%)
Protein (g/L)					
<= 45 g/L	0/181	0/75	0/180	0/75	0/330
>= 100 g/L	0/181	0/75	0/180	0/75	0/330
Prothrombin Intl. Normalized Ratio					
> 1.5 x ULN	2/167 (1.2%)	2/71 (2.8%)	1/172 (0.6%)	0/66	3/309 (1.0%)
Sodium (mmol/L)					
< 130 mmol/L	0/181	0/75	0/180	1/75 (1.3%)	1/330 (0.3%)
> 150 mmol/L	0/181	0/75	0/180	0/75	0/330
Urate (umol/L)					
> 595 umol/L for male, > 476 umol/L for female	2/181 (1.1%)	2/75 (2.7%)	3/180 (1.7%)	3/75 (4.0%)	8/330 (2.4%)
Urea Nitrogen (mmol/L)					
>= 10.7 mmol/L	1/181 (0.6%)	0/75	2/180 (1.1%)	1/75 (1.3%)	3/330 (0.9%)

- Abbreviations: bid, Twice a day; ULN, upper limit of the normal range
- m is the total number of patients with at least one post-baseline value.
- n and % are respectively the number and percentage of patients meeting the specified criteria at least once post-baseline.

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Table S-093 Summary of Markedly Abnormal Post-Baseline Laboratory Values in 52-Week Long-term Period with Monotherapy and Combination Therapy (PXL008-019; Long-term Safety Population)

Parameter Criteria	Imeglimin N = 134 n/m (%)	Imeglimin + SU N = 127 n/m (%)	Imeglimin + GLIN N = 64 n/m (%)	Imeglimin + BIG N = 64 n/m (%)	Imeglimin + AGI N = 64 n/m (%)	Imeglimin + TZD N = 65 n/m (%)	Imeglimin + DPP4-I N = 63 n/m (%)	Imeglimin + GLP1-RA N = 70 n/m (%)	Imeglimin + SGLT2-I N = 63 n/m (%)	Combination Total N = 580 n/m (%)	Imeglimin Total N = 714 n/m (%)
Activated Partial Thromboplastin Time (sec)											
> 1.5 x ULN	1/130 (0.8%)	0/121	0/62	0/61	0/62	0/65	0/61	0/68	0/63	0/563	1/693 (0.1%)
Alanine Aminotransferase (U/L)											
>= 3 x ULN	1/134 (0.7%)	1/127 (0.8%)	0/64	0/64	2/64 (3.1%)	0/65	1/63 (1.6%)	0/70	2/63 (3.2%)	6/580 (1.0%)	7/714 (1.0%)
Albumin (g/L)											
<= 25 g/L	0/134	0/127	0/64	0/64	0/64	0/65	0/63	0/70	0/63	0/580	0/714
Alkaline Phosphatase (U/L)											
>= 1.5 x ULN	0/134	0/127	0/64	1/64 (1.6%)	0/64	1/65 (1.5%)	0/63	0/70	0/63	2/580 (0.3%)	2/714 (0.3%)
Aspartate Aminotransferase (U/L)											
>= 3 x ULN	1/134 (0.7%)	0/127	0/64	0/64	1/64 (1.6%)	0/65	1/63 (1.6%)	1/70 (1.4%)	1/63 (1.6%)	4/580 (0.7%)	5/714 (0.7%)
Basophils (10^9/L)											
> 1.6 x 10^9/L	0/134	0/127	0/64	0/64	0/64	0/65	0/63	0/70	0/63	0/580	0/714
Basophils/Leukocytes (%)											
>= 10%	0/134	0/127	0/64	0/64	0/64	0/65	0/63	0/70	0/63	0/580	0/714

Parameter Criteria	Imeglimin N = 134 n/m (%)	Imeglimin + SU N = 127 n/m (%)	Imeglimin + GLIN N = 64 n/m (%)	Imeglimin + BIG N = 64 n/m (%)	Imeglimin + AGI N = 64 n/m (%)	Imeglimin + TZD N = 65 n/m (%)	Imeglimin + DPP4-I N = 63 n/m (%)	Imeglimin + GLP1-RA N = 70 n/m (%)	Imeglimin + SGLT2-I N = 63 n/m (%)	Combination Total N = 580 n/m (%)	Imeglimin Total N = 714 n/m (%)
Bilirubin (umol/L)											
>= 34.2 umol/L or > 2 x ULN	2/134 (1.5%)	3/127 (2.4%)	1/64 (1.6%)	1/64 (1.6%)	0/64	0/65	0/63	1/70 (1.4%)	1/63 (1.6%)	7/580 (1.2%)	9/714 (1.3%)
Calcium (mmol/L)											
< 1.75 mmol/L	1/134 (0.7%)	0/127	0/64	0/64	0/64	0/65	0/63	0/70	0/63	0/580	1/714 (0.1%)
>= 3.1 mmol/L	0/134	0/127	0/64	0/64	0/64	0/65	0/63	0/70	0/63	0/580	0/714
Chloride (mmol/L)											
<= 90 mmol/L	1/134 (0.7%)	1/127 (0.8%)	0/64	0/64	0/64	0/65	0/63	0/70	2/63 (3.2%)	3/580 (0.5%)	4/714 (0.6%)
>= 118 mmol/L	0/134	0/127	0/64	0/64	0/64	0/65	0/63	0/70	0/63	0/580	0/714
Creatine Kinase (U/L)											
> 2.5 x ULN	7/134 (5.2%)	4/127 (3.1%)	3/64 (4.7%)	0/64	3/64 (4.7%)	3/65 (4.6%)	2/63 (3.2%)	2/70 (2.9%)	1/63 (1.6%)	18/580 (3.1%)	25/714 (3.5%)
Creatinine (umol/L)											
>= 177 umol/L	0/134	0/127	0/64	0/64	0/64	0/65	0/63	0/70	0/63	0/580	0/714
Eosinophils (10^9/L)											
> 1.6 x 10^9/L	0/134	0/127	0/64	1/64 (1.6%)	0/64	0/65	0/63	0/70	0/63	1/580 (0.2%)	1/714 (0.1%)
Eosinophils/Leukocytes (%)											
>= 10%	4/134 (3.0%)	2/127 (1.6%)	1/64 (1.6%)	1/64 (1.6%)	3/64 (4.7%)	1/65 (1.5%)	0/63	2/70 (2.9%)	0/63	10/580 (1.7%)	14/714 (2.0%)
Erythrocytes (10^12/L)											

Parameter Criteria	Imeglimin N = 134 n/m (%)	Imeglimin + SU N = 127 n/m (%)	Imeglimin + GLIN N = 64 n/m (%)	Imeglimin + BIG N = 64 n/m (%)	Imeglimin + AGI N = 64 n/m (%)	Imeglimin + TZD N = 65 n/m (%)	Imeglimin + DPP4-I N = 63 n/m (%)	Imeglimin + GLP1-RA N = 70 n/m (%)	Imeglimin + SGLT2-I N = 63 n/m (%)	Combination Total N = 580 n/m (%)	Imeglimin Total N = 714 n/m (%)
<= 3.5 x 10^12/L	2/134 (1.5%)	6/127 (4.7%)	0/64	3/64 (4.7%)	0/64	3/65 (4.6%)	4/63 (6.3%)	1/70 (1.4%)	1/63 (1.6%)	18/580 (3.1%)	20/714 (2.8%)
>= 6.4 x 10^12/L	1/134 (0.7%)	0/127	0/64	0/64	0/64	0/65	0/63	0/70	0/63	0/580	1/714 (0.1%)
Gamma Glutamyl Transferase (U/L)											
>= 2.5 x ULN	8/134 (6.0%)	6/127 (4.7%)	2/64 (3.1%)	4/64 (6.3%)	3/64 (4.7%)	1/65 (1.5%)	5/63 (7.9%)	5/70 (7.1%)	7/63 (11.1%)	33/580 (5.7%)	41/714 (5.7%)
Hematocrit (fraction of 1)											
<= 0.37 for male, <= 0.32 for female	11/134 (8.2%)	11/127 (8.7%)	7/64 (10.9%)	12/64 (18.8%)	5/64 (7.8%)	12/65 (18.5%)	3/63 (4.8%)	3/70 (4.3%)	1/63 (1.6%)	54/580 (9.3%)	65/714 (9.1%)
>= 0.60 for male, >= 0.54 for female	1/134 (0.7%)	0/127	0/64	0/64	0/64	0/65	0/63	0/70	0/63	0/580	1/714 (0.1%)
Hemoglobin (g/L)											
<= 115 g/L for male, <= 95 g/L for female	4/134 (3.0%)	2/127 (1.6%)	1/64 (1.6%)	2/64 (3.1%)	2/64 (3.1%)	4/65 (6.2%)	1/63 (1.6%)	1/70 (1.4%)	0/63	13/580 (2.2%)	17/714 (2.4%)
>= 190 g/L for male, >= 175 g/L for female	1/134 (0.7%)	0/127	0/64	0/64	0/64	0/65	0/63	0/70	1/63 (1.6%)	1/580 (0.2%)	2/714 (0.3%)
Lactic Acid (mmol/L)											
> 5 mmol/L	0/130	1/122 (0.8%)	0/62	0/64	0/63	0/65	0/60	0/69	1/63 (1.6%)	2/568 (0.4%)	2/698 (0.3%)
Leukocytes (10^9/L)											
<= 2.8 x 10^9/L	3/134 (2.2%)	3/127 (2.4%)	1/64 (1.6%)	0/64	3/64 (4.7%)	4/65 (6.2%)	1/63 (1.6%)	0/70	0/63	12/580 (2.1%)	15/714 (2.1%)
>= 16 x 10^9/L	0/134	1/127 (0.8%)	0/64	0/64	0/64	1/65 (1.5%)	0/63	0/70	0/63	2/580 (0.3%)	2/714 (0.3%)

Parameter Criteria	Imeglimin N = 134 n/m (%)	Imeglimin + SU N = 127 n/m (%)	Imeglimin + GLIN N = 64 n/m (%)	Imeglimin + BIG N = 64 n/m (%)	Imeglimin + AGI N = 64 n/m (%)	Imeglimin + TZD N = 65 n/m (%)	Imeglimin + DPP4-I N = 63 n/m (%)	Imeglimin + GLP1-RA N = 70 n/m (%)	Imeglimin + SGLT2-I N = 63 n/m (%)	Combination Total N = 580 n/m (%)	Imeglimin Total N = 714 n/m (%)
Lipase (U/L)											
>= 3 x ULN	2/134 (1.5%)	2/127 (1.6%)	0/64	1/64 (1.6%)	2/64 (3.1%)	1/65 (1.5%)	2/63 (3.2%)	0/70	1/63 (1.6%)	9/580 (1.6%)	11/714 (1.5%)
Lymphocytes (10^9/L)											
> 12 x 10^9/L	0/134	0/127	0/64	0/64	0/64	0/65	0/63	0/70	0/63	0/580	0/714
Lymphocytes/Leukocytes (%)											
>= 75%	0/134	0/127	0/64	0/64	0/64	0/65	0/63	0/70	0/63	0/580	0/714
Monocytes (10^9/L)											
> 2.5 x 10^9/L	0/134	0/127	0/64	0/64	0/64	0/65	0/63	0/70	0/63	0/580	0/714
Monocytes/Leukocytes (%)											
>= 15%	1/134 (0.7%)	0/127	0/64	1/64 (1.6%)	1/64 (1.6%)	0/65	0/63	0/70	0/63	2/580 (0.3%)	3/714 (0.4%)
Neutrophils (10^9/L)											
< 0.5 x 10^9/L	0/134	0/127	0/64	0/64	0/64	0/65	0/63	0/70	0/63	0/580	0/714
> 13.5 x 10^9/L	0/134	1/127 (0.8%)	0/64	0/64	0/64	1/65 (1.5%)	0/63	0/70	0/63	2/580 (0.3%)	2/714 (0.3%)
Neutrophils/Leukocytes (%)											
<= 15%	0/134	0/127	0/64	0/64	0/64	0/65	0/63	0/70	0/63	0/580	0/714
> 85%	1/134 (0.7%)	2/127 (1.6%)	0/64	1/64 (1.6%)	0/64	0/65	0/63	1/70 (1.4%)	0/63	4/580 (0.7%)	5/714 (0.7%)
Phosphate (mmol/L)											

Parameter Criteria	Imeglimin N = 134 n/m (%)	Imeglimin + SU N = 127 n/m (%)	Imeglimin + GLIN N = 64 n/m (%)	Imeglimin + BIG N = 64 n/m (%)	Imeglimin + AGI N = 64 n/m (%)	Imeglimin + TZD N = 65 n/m (%)	Imeglimin + DPP4-I N = 63 n/m (%)	Imeglimin + GLP1-RA N = 70 n/m (%)	Imeglimin + SGLT2-I N = 63 n/m (%)	Combination Total N = 580 n/m (%)	Imeglimin Total N = 714 n/m (%)
< 0.65 mmol/L	0/134	0/127	0/64	0/64	1/64 (1.6%)	0/65	0/63	1/70 (1.4%)	0/63	2/580 (0.3%)	2/714 (0.3%)
> 1.65 mmol/L	0/134	0/127	0/64	1/64 (1.6%)	0/64	0/65	2/63 (3.2%)	1/70 (1.4%)	0/63	4/580 (0.7%)	4/714 (0.6%)
Platelets (10^9/L)											
<= 75 x 10^9/L	0/134	1/127 (0.8%)	0/64	1/64 (1.6%)	0/63	0/65	0/63	0/70	0/63	2/579 (0.3%)	2/713 (0.3%)
>= 700 x 10^9/L	0/134	0/127	0/64	0/64	0/63	0/65	0/63	0/70	0/63	0/579	0/713
Potassium (mmol/L)											
< 3 mmol/L	0/134	0/127	0/64	0/64	0/64	0/65	0/63	0/70	1/63 (1.6%)	1/580 (0.2%)	1/714 (0.1%)
> 5.5 mmol/L	2/134 (1.5%)	3/127 (2.4%)	2/64 (3.1%)	0/64	0/64	2/65 (3.1%)	2/63 (3.2%)	1/70 (1.4%)	3/63 (4.8%)	13/580 (2.2%)	15/714 (2.1%)
Protein (g/L)											
<= 45 g/L	0/134	0/127	0/64	0/64	0/64	0/65	0/63	0/70	0/63	0/580	0/714
>= 100 g/L	0/134	0/127	0/64	0/64	0/64	0/65	0/63	0/70	0/63	0/580	0/714
Prothrombin Intl. Normalized Ratio											
> 1.5 x ULN	0/130	0/121	0/62	0/61	0/62	0/65	0/61	0/68	0/63	0/563	0/693
Sodium (mmol/L)											
< 130 mmol/L	0/134	0/127	0/64	0/64	0/64	0/65	0/63	0/70	0/63	0/580	0/714
> 150 mmol/L	0/134	0/127	0/64	0/64	0/64	0/65	0/63	0/70	0/63	0/580	0/714
Urate (umol/L)											

Parameter Criteria	Imeglimin N = 134 n/m (%)	Imeglimin + SU N = 127 n/m (%)	Imeglimin + GLIN N = 64 n/m (%)	Imeglimin + BIG N = 64 n/m (%)	Imeglimin + AGI N = 64 n/m (%)	Imeglimin + TZD N = 65 n/m (%)	Imeglimin + DPP4-I N = 63 n/m (%)	Imeglimin + GLP1-RA N = 70 n/m (%)	Imeglimin + SGLT2-I N = 63 n/m (%)	Combination Total N = 580 n/m (%)	Imeglimin Total N = 714 n/m (%)
> 595 umol/L for male, > 476 umol/L for female	1/134 (0.7%)	0/127	0/64	1/64 (1.6%)	0/64	2/65 (3.1%)	1/63 (1.6%)	1/70 (1.4%)	0/63	5/580 (0.9%)	6/714 (0.8%)
Urea Nitrogen (mmol/L)											
>= 10.7 mmol/L	1/134 (0.7%)	1/127 (0.8%)	0/64	2/64 (3.1%)	1/64 (1.6%)	1/65 (1.5%)	1/63 (1.6%)	1/70 (1.4%)	0/63	7/580 (1.2%)	8/714 (1.1%)

- Abbreviations: ULN, upper limit of the normal range; SU, Sulphonylurea; GLIN, Glinide; BIG, Biguanide; AGI, Alpha glucosidase inhibitor; TZD, Thiazolidinedione; DPP4-I, Dipeptidyl peptidase-4 inhibitor; GLP1-RA, Glucagon-like peptide 1 receptor agonist; SGLT2-I, Sodium glucose cotransporter 2 inhibitor
- "Imeglimin" in this table means "Imeglimin 1000 mg twice daily".
- "Combination Total" is the sum of the subjects excluding monotherapy "Imeglimin".
- "Imeglimin Total" is the sum of all subjects in Imeglimin treatment groups.
- m is the total number of patients with at least one post-baseline value.
- n and % are respectively the number and percentage of patients meeting the specified criteria at least once post-baseline.

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Table S-094 Summary of Markedly Abnormal Post-Baseline Laboratory Values in 16-Week Double-blind Period in Combination with Insulin Therapy (PXL008-020; Safety Population)

Parameter Criteria	Placebo + Insulin N = 107 n/m (%)	Imeglimin 1000 mg bid + Insulin N = 108 n/m (%)
Activated Partial Thromboplastin Time (sec)		
> 1.5 x ULN	0/102	0/105
Alanine Aminotransferase (U/L)		
>= 3 x ULN	0/106	0/108
Albumin (g/L)		
<= 25 g/L	0/106	0/108
Alkaline Phosphatase (U/L)		
>= 1.5 x ULN	0/106	1/108 (0.9%)
Aspartate Aminotransferase (U/L)		
>= 3 x ULN	0/106	0/108
Basophils (10^9/L)		
> 1.6 x 10^9/L	0/106	0/108
Basophils/Leukocytes (%)		
>= 10%	0/106	0/108
Bilirubin (umol/L)		
>= 34.2 umol/L or > 2 x ULN	1/106 (0.9%)	0/108
Calcium (mmol/L)		
< 1.75 mmol/L	0/106	0/108
>= 3.1 mmol/L	0/106	0/108
Chloride (mmol/L)		
<= 90 mmol/L	0/106	0/108
>= 118 mmol/L	0/106	0/108
Creatine Kinase (U/L)		
> 2.5 x ULN	0/106	1/108 (0.9%)
Creatinine (umol/L)		
>= 177 umol/L	0/106	0/108
Eosinophils (10^9/L)		
> 1.6 x 10^9/L	0/106	0/108
Eosinophils/Leukocytes (%)		
>= 10%	0/106	0/108
Erythrocytes (10^12/L)		
<= 3.5 x 10^12/L	1/106 (0.9%)	0/108
>= 6.4 x 10^12/L	0/106	1/108 (0.9%)

Parameter Criteria	Placebo + Insulin N = 107 n/m (%)	Imeglimin 1000 mg bid + Insulin N = 108 n/m (%)
Gamma Glutamyl Transferase (U/L)		
>= 2.5 x ULN	1/106 (0.9%)	2/108 (1.9%)
Hematocrit (fraction of 1)		
<= 0.37 for male, <= 0.32 for female	3/106 (2.8%)	3/108 (2.8%)
>= 0.60 for male, >= 0.54 for female	0/106	0/108
Hemoglobin (g/L)		
<= 115 g/L for male, <= 95 g/L for female	0/106	0/108
>= 190 g/L for male, >= 175 g/L for female	0/106	0/108
Lactic Acid (mmol/L)		
> 5 mmol/L	0/104	1/108 (0.9%)
Leukocytes (10^9/L)		
<= 2.8 x 10^9/L	2/106 (1.9%)	0/108
>= 16 x 10^9/L	0/106	0/108
Lipase (U/L)		
>= 3 x ULN	1/106 (0.9%)	0/108
Lymphocytes (10^9/L)		
> 12 x 10^9/L	0/106	0/108
Lymphocytes/Leukocytes (%)		
>= 75%	0/106	0/108
Monocytes (10^9/L)		
> 2.5 x 10^9/L	0/106	0/108
Monocytes/Leukocytes (%)		
>= 15%	0/106	0/108
Neutrophils (10^9/L)		
< 0.5 x 10^9/L	0/106	0/108
> 13.5 x 10^9/L	0/106	0/108
Neutrophils/Leukocytes (%)		
<= 15%	0/106	0/108
> 85%	0/106	0/108
Phosphate (mmol/L)		
< 0.65 mmol/L	0/106	0/108
> 1.65 mmol/L	0/106	1/108 (0.9%)
Platelets (10^9/L)		
<= 75 x 10^9/L	0/106	0/108
>= 700 x 10^9/L	0/106	0/108

Parameter Criteria	Placebo + Insulin N = 107 n/m (%)	Imeglimin 1000 mg bid + Insulin N = 108 n/m (%)
Potassium (mmol/L)		
< 3 mmol/L	0/106	0/108
> 5.5 mmol/L	1/106 (0.9%)	0/108
Protein (g/L)		
<= 45 g/L	0/106	0/108
>= 100 g/L	0/106	0/108
Prothrombin Intl. Normalized Ratio		
> 1.5 x ULN	0/102	0/105
Sodium (mmol/L)		
< 130 mmol/L	1/106 (0.9%)	0/108
> 150 mmol/L	0/106	0/108
Urate (umol/L)		
> 595 umol/L for male, > 476 umol/L for female	0/106	0/108
Urea Nitrogen (mmol/L)		
>= 10.7 mmol/L	1/106 (0.9%)	1/108 (0.9%)

- Abbreviations: bid, Twice a day; ULN, upper limit of the normal range
- m is the total number of patients with at least one post-baseline value.
- n and % are respectively the number and percentage of patients meeting the specified criteria at least once post-baseline.

Control No:<<t-s-094-labot-020db.sas, 2020-03-06T00:11:32>>

Table S-095 Summary of Markedly Abnormal Post-Baseline Laboratory Values in 52-Week Long-term Period in Combination with Insulin Therapy (PXL008-020; Long-term Safety Population)

Parameter Criteria	Placebo/Imeglimin + Insulin N = 101 n/m (%)	Imeglimin/Imeglimin + Insulin N = 108 n/m (%)	Imeglimin + Insulin Total N = 209 n/m (%)
Activated Partial Thromboplastin Time (sec)			
> 1.5 x ULN	0/99	0/108	0/207
Alanine Aminotransferase (U/L)			
>= 3 x ULN	0/101	0/108	0/209
Albumin (g/L)			
<= 25 g/L	0/101	0/108	0/209
Alkaline Phosphatase (U/L)			
>= 1.5 x ULN	0/101	1/108 (0.9%)	1/209 (0.5%)
Aspartate Aminotransferase (U/L)			
>= 3 x ULN	0/101	1/108 (0.9%)	1/209 (0.5%)
Basophils (10^9/L)			
> 1.6 x 10^9/L	0/101	0/108	0/209
Basophils/Leukocytes (%)			
>= 10%	0/101	0/108	0/209
Bilirubin (umol/L)			
>= 34.2 umol/L or > 2 x ULN	0/101	0/108	0/209
Calcium (mmol/L)			
< 1.75 mmol/L	0/101	0/108	0/209
>= 3.1 mmol/L	0/101	0/108	0/209
Chloride (mmol/L)			
<= 90 mmol/L	0/101	0/108	0/209
>= 118 mmol/L	0/101	0/108	0/209
Creatine Kinase (U/L)			
> 2.5 x ULN	2/101 (2.0%)	6/108 (5.6%)	8/209 (3.8%)
Creatinine (umol/L)			
>= 177 umol/L	0/101	0/108	0/209
Eosinophils (10^9/L)			
> 1.6 x 10^9/L	0/101	0/108	0/209
Eosinophils/Leukocytes (%)			
>= 10%	1/101 (1.0%)	1/108 (0.9%)	2/209 (1.0%)
Erythrocytes (10^12/L)			

Parameter Criteria	Placebo/Imeglimin + Insulin N = 101 n/m (%)	Imeglimin/Imeglimin + Insulin N = 108 n/m (%)	Imeglimin + Insulin Total N = 209 n/m (%)
<= 3.5 x 10^12/L	1/101 (1.0%)	1/108 (0.9%)	2/209 (1.0%)
>= 6.4 x 10^12/L	0/101	1/108 (0.9%)	1/209 (0.5%)
Gamma Glutamyl Transferase (U/L)			
>= 2.5 x ULN	1/101 (1.0%)	4/108 (3.7%)	5/209 (2.4%)
Hematocrit (fraction of 1)			
<= 0.37 for male, <= 0.32 for female	3/101 (3.0%)	7/108 (6.5%)	10/209 (4.8%)
>= 0.60 for male, >= 0.54 for female	0/101	0/108	0/209
Hemoglobin (g/L)			
<= 115 g/L for male, <= 95 g/L for female	0/101	0/108	0/209
>= 190 g/L for male, >= 175 g/L for female	0/101	0/108	0/209
Lactic Acid (mmol/L)			
> 5 mmol/L	0/99	1/108 (0.9%)	1/207 (0.5%)
Leukocytes (10^9/L)			
<= 2.8 x 10^9/L	2/101 (2.0%)	1/108 (0.9%)	3/209 (1.4%)
>= 16 x 10^9/L	0/101	0/108	0/209
Lipase (U/L)			
>= 3 x ULN	1/101 (1.0%)	0/108	1/209 (0.5%)
Lymphocytes (10^9/L)			
> 12 x 10^9/L	0/101	0/108	0/209
Lymphocytes/Leukocytes (%)			
>= 75%	0/101	0/108	0/209
Monocytes (10^9/L)			
> 2.5 x 10^9/L	0/101	0/108	0/209
Monocytes/Leukocytes (%)			
>= 15%	0/101	0/108	0/209
Neutrophils (10^9/L)			
< 0.5 x 10^9/L	0/101	0/108	0/209
> 13.5 x 10^9/L	0/101	0/108	0/209
Neutrophils/Leukocytes (%)			
<= 15%	0/101	0/108	0/209
> 85%	1/101 (1.0%)	0/108	1/209 (0.5%)
Phosphate (mmol/L)			
< 0.65 mmol/L	0/101	0/108	0/209
> 1.65 mmol/L	0/101	2/108 (1.9%)	2/209 (1.0%)

Parameter Criteria	Placebo/Imeglimin + Insulin N = 101 n/m (%)	Imeglimin/Imeglimin + Insulin N = 108 n/m (%)	Imeglimin + Insulin Total N = 209 n/m (%)
Platelets (10^9/L)			
<= 75 x 10^9/L	0/101	0/108	0/209
>= 700 x 10^9/L	0/101	0/108	0/209
Potassium (mmol/L)			
< 3 mmol/L	0/101	0/108	0/209
> 5.5 mmol/L	1/101 (1.0%)	1/108 (0.9%)	2/209 (1.0%)
Protein (g/L)			
<= 45 g/L	0/101	0/108	0/209
>= 100 g/L	0/101	0/108	0/209
Prothrombin Intl. Normalized Ratio			
> 1.5 x ULN	0/99	0/108	0/207
Sodium (mmol/L)			
< 130 mmol/L	0/101	0/108	0/209
> 150 mmol/L	0/101	0/108	0/209
Urate (umol/L)			
> 595 umol/L for male, > 476 umol/L for female	0/101	0/108	0/209
Urea Nitrogen (mmol/L)			
>= 10.7 mmol/L	1/101 (1.0%)	2/108 (1.9%)	3/209 (1.4%)

- Abbreviations: ULN, upper limit of the normal range
- "Imeglimin" in this table means "Imeglimin 1000 mg twice daily".
- The Long-term Safety Population excludes data during administration of placebo in the double-blind period.
- "Imeglimin + Insulin Total" is the sum of subjects in the placebo group in the open-label period and Imeglimin group in the double-blind and open-label periods.
- m is the total number of patients with at least one post-baseline value.
- n and % are respectively the number and percentage of patients meeting the specified criteria at least once post-baseline.

Control No:<<t-s-095-labot-020lt.sas, 2020-03-06T00:10:31>>

Table S-097 Summary of Change from Baseline in eGFR (mL/min/1.73m2) to Week 24 in 24-Week Double-blind Period with Monotherapy (PXL008-014, PXL008-018; Safety Population)

Parameter	Observed			Change from baseline	
Treatment Visit	n	Mean (SD)	Median [Min, Max]	Mean (SD)	Median [Min, Max]
eGFR (mL/min/1.73m2)					
Placebo (N = 182)					
Baseline	182	71.5014 (12.40252)	69.3015 [49.175, 109.000]		
Week 24	167	71.8462 (13.10878)	70.4350 [45.683, 105.000]	0.2889 (8.77913)	-0.2970 [-29.091, 27.544]
LOCF Endpoint	167	71.8462 (13.10878)	70.4350 [45.683, 105.000]	0.2889 (8.77913)	-0.2970 [-29.091, 27.544]
Imeglimin 500 mg bid (N = 75)					
Baseline	75	73.8000 (12.56443)	73.0000 [50.000, 101.000]		
Week 24	70	72.1714 (11.62577)	72.0000 [47.000, 102.000]	-1.8143 (6.67961)	-2.0000 [-21.000, 11.000]
LOCF Endpoint	70	72.1714 (11.62577)	72.0000 [47.000, 102.000]	-1.8143 (6.67961)	-2.0000 [-21.000, 11.000]
Imeglimin 1000 mg bid (N = 180)					
Baseline	180	73.5632 (12.76615)	73.4670 [45.156, 115.412]		
Week 24	168	71.9390 (13.50996)	70.9615 [43.013, 112.000]	-1.4464 (9.38032)	-0.3785 [-29.267, 21.000]
LOCF Endpoint	168	71.9390 (13.50996)	70.9615 [43.013, 112.000]	-1.4464 (9.38032)	-0.3785 [-29.267, 21.000]
Imeglimin 1500 mg bid (N = 75)					
Baseline	75	75.2400 (15.16026)	73.0000 [48.000, 117.000]		
Week 24	67	73.2836 (14.45034)	71.0000 [51.000, 114.000]	-1.9403 (8.18143)	-2.0000 [-19.000, 21.000]
LOCF Endpoint	67	73.2836 (14.45034)	71.0000 [51.000, 114.000]	-1.9403 (8.18143)	-2.0000 [-19.000, 21.000]

- Abbreviations: bid, Twice a day; SD, standard deviation; LOCF, Last Observation Carried Forward; eGFR, Estimated Glomerular Filtration Rate

Control No:<<t-s-097-labot-24wdb.sas, 2020-03-06T00:10:43>>

Table S-099 Summary of Change from Baseline in Weight (kg) at All Visits in 24-Week Double-blind Period with Monotherapy (PXL008-014, PXL008-018; Safety Population)

Parameter	Observed			Change from baseline	
Treatment Visit	n	Mean (SD)	Median [Min, Max]	Mean (SD)	Median [Min, Max]
Weight (kg)					
Placebo (N = 182)					
Baseline	182	69.74 (13.668)	67.90 [40.2, 113.2]		
Week 2	74	70.13 (14.813)	67.65 [41.7, 107.5]	-0.17 (0.770)	-0.10 [-2.7, 2.0]
Week 4	180	69.60 (13.773)	67.70 [41.5, 113.5]	-0.16 (0.897)	-0.10 [-4.3, 2.0]
Week 8	176	69.61 (13.746)	67.85 [41.1, 113.0]	-0.15 (1.142)	-0.10 [-4.2, 2.6]
Week 12	169	69.82 (13.705)	68.10 [40.7, 113.1]	-0.23 (1.271)	-0.30 [-7.1, 3.0]
Week 16	168	69.58 (13.546)	67.80 [40.8, 112.0]	-0.38 (1.358)	-0.30 [-8.6, 3.1]
Week 20	168	69.60 (13.447)	67.70 [40.6, 112.3]	-0.35 (1.602)	-0.20 [-10.4, 3.2]
Week 24	167	69.56 (13.518)	68.20 [39.7, 112.4]	-0.41 (1.653)	-0.20 [-11.9, 3.2]
LOCF Endpoint	182	69.27 (13.483)	67.90 [39.7, 112.4]	-0.47 (1.678)	-0.25 [-11.9, 3.2]
Imeglimin 500 mg bid (N = 75)					
Baseline	75	68.51 (15.183)	67.00 [35.6, 115.8]		
Week 2	75	68.44 (15.148)	68.10 [35.4, 115.8]	-0.07 (0.688)	-0.10 [-1.8, 2.2]
Week 4	75	68.47 (15.238)	67.40 [34.9, 114.2]	-0.05 (0.725)	0.00 [-1.7, 2.1]
Week 8	72	67.79 (14.868)	66.95 [35.3, 114.9]	-0.08 (0.979)	-0.15 [-3.4, 2.5]
Week 12	72	67.84 (14.779)	65.50 [36.1, 114.1]	-0.03 (1.070)	-0.10 [-2.5, 3.5]
Week 16	71	67.77 (14.851)	65.40 [36.3, 115.5]	-0.14 (1.406)	-0.20 [-4.3, 3.4]
Week 20	70	67.65 (14.575)	65.55 [36.8, 114.1]	0.11 (1.818)	-0.10 [-6.1, 4.7]
Week 24	70	67.74 (14.683)	65.75 [37.0, 115.0]	0.20 (2.037)	0.25 [-6.3, 4.9]
LOCF Endpoint	75	68.62 (14.802)	66.20 [37.0, 115.0]	0.11 (2.054)	0.20 [-6.3, 4.9]
Imeglimin 1000 mg bid (N = 180)					
Baseline	180	69.65 (13.548)	68.90 [42.5, 124.0]		
Week 2	73	67.53 (12.650)	66.60 [45.2, 97.1]	-0.04 (0.635)	0.00 [-1.6, 1.6]
Week 4	178	69.45 (13.699)	68.25 [42.3, 123.0]	-0.13 (0.852)	-0.10 [-3.0, 2.0]
Week 8	175	69.41 (13.811)	68.30 [41.2, 122.3]	-0.24 (1.012)	-0.20 [-3.8, 3.0]
Week 12	172	69.40 (13.971)	68.30 [41.5, 124.1]	-0.25 (1.149)	-0.20 [-4.9, 2.8]
Week 16	171	69.24 (13.827)	68.30 [41.8, 121.5]	-0.27 (1.410)	-0.20 [-5.9, 4.8]
Week 20	169	69.09 (13.762)	67.50 [42.0, 124.3]	-0.16 (1.432)	-0.20 [-5.9, 4.9]
Week 24	169	69.35 (13.811)	67.90 [40.9, 123.7]	-0.20 (1.572)	-0.20 [-6.9, 5.8]
LOCF Endpoint	180	69.44 (13.731)	68.40 [40.9, 123.7]	-0.21 (1.552)	-0.20 [-6.9, 5.8]
Imeglimin 1500 mg bid (N = 75)					
Baseline	75	73.13 (15.486)	73.00 [41.5, 122.3]		
Week 2	71	73.98 (15.476)	74.20 [40.8, 124.0]	0.01 (0.913)	0.00 [-1.9, 2.2]
Week 4	70	74.03 (15.636)	74.30 [40.7, 123.9]	0.02 (0.946)	0.00 [-1.9, 2.0]
Week 8	68	73.93 (15.870)	74.25 [40.3, 123.9]	-0.19 (1.397)	-0.30 [-4.1, 2.6]
Week 12	68	73.85 (16.102)	73.70 [40.2, 123.8]	-0.27 (1.683)	-0.25 [-4.8, 3.2]
Week 16	68	73.96 (16.084)	74.00 [39.8, 124.6]	-0.16 (1.830)	-0.15 [-4.3, 4.3]
Week 20	67	74.52 (15.852)	73.90 [40.1, 126.3]	0.00 (1.849)	0.20 [-4.6, 4.0]
Week 24	67	74.59 (15.903)	74.90 [40.4, 125.2]	0.07 (2.028)	0.00 [-3.6, 4.8]
LOCF Endpoint	75	73.10 (16.025)	72.30 [40.4, 125.2]	-0.03 (1.972)	0.00 [-3.6, 4.8]

- Abbreviations: bid, Twice a day; SD, standard deviation; LOCF, Last Observation Carried Forward

Control No:<<t-s-099-vsign-24wdb.sas, 2020-03-06T00:10:25>>

Table S-101 Summary of Change from Baseline in eGFR (mL/min/1.73m2) to Week 52 in 52-Week Long-term Period with Monotherapy and Combination Therapy (PXL008-019; Long-term Safety Population)

Parameter	Observed			Change from baseline	
Treatment Visit	n	Mean (SD)	Median [Min, Max]	Mean (SD)	Median [Min, Max]
eGFR (mL/min/1.73m2)					
Imeglimin (N = 134)					
Baseline	134	75.9410 (15.46019)	74.7075 [50.434, 128.497]		
Week 24	130	72.3896 (13.28905)	73.1265 [46.572, 115.118]	-3.4694 (9.11293)	-0.4190 [-30.446, 20.329]
Week 52	126	72.4544 (14.22207)	70.1010 [50.055, 136.265]	-3.0990 (9.06710)	-0.4140 [-39.999, 19.732]
LOCF Endpoint	130	72.5660 (14.18910)	70.2970 [50.055, 136.265]	-3.2930 (9.06185)	-0.4190 [-39.999, 19.732]
Imeglimin + SU (N = 127)					
Baseline	127	76.9823 (12.42985)	75.0670 [53.846, 109.147]		
Week 24	122	74.2767 (11.49198)	73.6195 [51.852, 101.669]	-2.8380 (8.90973)	-0.4190 [-28.217, 17.179]
Week 52	116	73.8374 (11.56177)	72.8780 [46.960, 101.669]	-2.9056 (8.58409)	-0.4165 [-29.905, 16.740]
LOCF Endpoint	122	73.9233 (11.86218)	72.8780 [46.960, 101.669]	-3.1913 (8.78206)	-0.4190 [-29.905, 16.740]
Imeglimin + GLIN (N = 64)					
Baseline	64	78.4059 (12.14961)	76.3985 [47.529, 106.850]		
Week 24	62	74.3704 (12.84109)	73.3200 [53.846, 107.971]	-3.8977 (8.37390)	-0.4840 [-32.271, 16.499]
Week 52	59	75.5495 (12.74618)	73.4630 [47.336, 107.971]	-3.1046 (10.46263)	-0.5000 [-32.271, 16.499]
LOCF Endpoint	62	75.2963 (12.58631)	73.3200 [47.336, 107.971]	-2.9717 (10.21942)	-0.4890 [-32.271, 16.499]
Imeglimin + BIG (N = 64)					
Baseline	64	82.6959 (18.27707)	78.6110 [53.846, 144.708]		
Week 24	61	76.7890 (15.72237)	75.7540 [38.444, 126.037]	-5.6222 (9.20373)	-1.6940 [-27.025, 15.319]
Week 52	58	77.1450 (15.08289)	76.2970 [57.064, 126.037]	-4.7974 (10.62783)	-0.5400 [-30.261, 20.247]
LOCF Endpoint	61	77.5969 (15.01979)	76.8400 [57.064, 126.037]	-4.8143 (10.47002)	-0.5370 [-30.261, 20.247]
Imeglimin + AGI (N = 64)					
Baseline	64	78.2605 (13.15447)	75.1270 [56.190, 126.681]		
Week 24	63	77.8086 (17.40138)	72.8640 [52.412, 126.101]	-0.5079 (9.99088)	-0.4590 [-16.266, 26.737]
Week 52	62	75.7807 (15.60646)	72.2775 [52.412, 126.101]	-2.2679 (8.43224)	-0.4840 [-17.300, 24.345]
LOCF Endpoint	63	75.8720 (15.49701)	72.5520 [52.412, 126.101]	-2.4445 (8.48063)	-0.4870 [-17.300, 24.345]
Imeglimin + TZD (N = 65)					
Baseline	65	79.6182 (15.32343)	77.6040 [54.517, 126.681]		

Parameter	Observed			Change from baseline	
Treatment Visit	n	Mean (SD)	Median [Min, Max]	Mean (SD)	Median [Min, Max]
Week 24	65	76.0783 (13.03293)	74.0860 [48.131, 114.507]	-3.5399 (11.34727)	-0.4340 [-39.413, 26.864]
Week 52	65	75.9019 (15.05440)	72.8640 [52.292, 114.507]	-3.7163 (10.03832)	-0.4790 [-27.213, 20.329]
LOCF Endpoint	65	75.9019 (15.05440)	72.8640 [52.292, 114.507]	-3.7163 (10.03832)	-0.4790 [-27.213, 20.329]
Imeglimin + DPP4-I (N = 63)					
Baseline	63	75.2570 (13.51408)	74.0860 [51.852, 123.045]		
Week 24	61	71.6404 (10.93784)	72.3360 [30.758, 101.991]	-3.4724 (10.62991)	-0.3630 [-44.483, 12.464]
Week 52	60	72.3039 (10.70771)	72.7380 [52.805, 101.991]	-2.9907 (10.60412)	-0.4285 [-44.483, 19.402]
LOCF Endpoint	61	72.0240 (10.84086)	72.6120 [52.805, 101.991]	-3.0888 (10.54323)	-0.4380 [-44.483, 19.402]
Imeglimin + GLP1-RA (N = 70)					
Baseline	70	79.5616 (14.70430)	76.2835 [54.750, 146.911]		
Week 24	69	77.0314 (13.42038)	75.3250 [51.639, 111.683]	-1.5541 (11.45324)	-0.4940 [-21.824, 27.729]
Week 52	66	76.2192 (13.05991)	74.2280 [54.502, 111.024]	-2.2831 (10.49134)	-0.4405 [-36.799, 16.673]
LOCF Endpoint	69	76.3024 (13.33905)	74.0860 [54.502, 111.024]	-2.2831 (10.59671)	-0.4470 [-36.799, 16.673]
Imeglimin + SGLT2-I (N = 63)					
Baseline	63	83.7246 (14.61521)	81.5280 [52.607, 116.376]		
Week 24	63	80.7316 (15.75646)	82.0470 [52.412, 114.223]	-2.9930 (11.36134)	-0.4910 [-42.006, 19.770]
Week 52	61	81.4239 (15.54236)	81.0470 [51.710, 129.129]	-2.3744 (11.67908)	-0.4690 [-27.596, 42.454]
LOCF Endpoint	63	81.1896 (15.65196)	81.0470 [51.710, 129.129]	-2.5350 (11.59113)	-0.4770 [-27.596, 42.454]

- Abbreviations: SD, standard deviation; LOCF, Last Observation Carried Forward; SU, Sulphonylurea; GLIN, Glinide; BIG, Biguanide; AGI, Alpha glucosidase inhibitor; TZD, Thiazolidinedione; DPP4-I, Dipeptidyl peptidase-4 inhibitor; GLP1-RA, Glucagon-like peptide 1 receptor agonist; SGLT2-I, Sodium glucose cotransporter 2 inhibitor; eGFR, Estimated Glomerular Filtration Rate
- "Imeglimin" in this table means "Imeglimin 1000 mg twice daily".

Control No:<<t-s-101-labot-019lt.sas, 2020-03-06T00:10:35>>

Table S-103 Summary of Change from Baseline in Weight (kg) at All Visits in 52-Week Long-term Period with Monotherapy and Combination Therapy (PXL008-019; Long-term Safety Population)

Parameter	Observed			Change from baseline	
Treatment Visit	n	Mean (SD)	Median [Min, Max]	Mean (SD)	Median [Min, Max]
Weight (kg)					
Imeglimin (N = 134)					
Baseline	134	71.02 (13.785)	69.10 [44.6, 129.0]		
Week 4	134	70.92 (13.701)	68.90 [45.0, 127.4]	-0.10 (0.997)	0.00 [-3.5, 3.1]
Week 8	132	70.78 (13.749)	68.73 [45.0, 130.2]	-0.14 (1.332)	-0.15 [-3.9, 3.7]
Week 12	131	70.55 (13.703)	68.40 [43.9, 130.4]	-0.23 (1.550)	-0.30 [-4.2, 3.8]
Week 16	130	70.57 (13.890)	68.45 [44.3, 134.2]	-0.37 (1.849)	-0.25 [-5.1, 5.2]
Week 20	130	70.47 (13.743)	68.30 [43.7, 133.0]	-0.47 (2.017)	-0.40 [-5.8, 5.6]
Week 24	130	70.27 (13.689)	68.03 [43.5, 133.0]	-0.67 (2.103)	-0.70 [-7.5, 4.2]
Week 28	129	70.43 (13.725)	68.30 [42.2, 130.8]	-0.57 (2.115)	-0.40 [-7.9, 4.3]
Week 32	128	70.51 (13.723)	68.75 [43.7, 130.6]	-0.45 (2.011)	-0.40 [-7.0, 4.0]
Week 36	128	70.56 (13.771)	69.00 [43.2, 131.6]	-0.40 (2.077)	-0.20 [-7.3, 4.0]
Week 40	128	70.72 (14.030)	68.50 [44.0, 132.6]	-0.25 (2.143)	0.00 [-7.4, 4.5]
Week 44	127	70.74 (14.188)	68.70 [43.2, 132.6]	-0.17 (2.217)	-0.10 [-7.9, 5.5]
Week 48	127	70.32 (14.019)	68.60 [42.9, 134.2]	-0.59 (2.307)	-0.40 [-9.1, 5.2]
Week 52	126	70.07 (13.846)	68.25 [43.1, 131.0]	-0.71 (2.410)	-0.60 [-9.2, 5.4]
LOCF Endpoint	134	70.24 (14.050)	68.25 [43.1, 131.0]	-0.78 (2.451)	-0.65 [-9.2, 5.4]
Imeglimin + SU (N = 127)					
Baseline	127	70.64 (13.761)	67.80 [44.3, 114.6]		
Week 4	127	70.91 (13.985)	67.90 [44.6, 118.2]	0.26 (1.011)	0.10 [-3.2, 4.0]
Week 8	126	70.94 (13.808)	68.05 [44.3, 116.1]	0.17 (1.162)	0.10 [-2.9, 3.7]
Week 12	123	70.94 (13.772)	68.20 [43.9, 116.7]	0.17 (1.393)	0.00 [-2.9, 4.3]
Week 16	123	71.01 (13.727)	68.50 [44.3, 116.3]	0.24 (1.593)	0.10 [-3.8, 7.3]
Week 20	123	71.17 (13.759)	68.00 [43.0, 116.2]	0.39 (1.643)	0.40 [-4.6, 7.0]
Week 24	122	71.32 (13.739)	69.05 [44.1, 116.0]	0.42 (1.613)	0.60 [-5.9, 4.2]
Week 28	122	71.38 (13.712)	68.95 [44.1, 114.3]	0.47 (1.731)	0.50 [-4.2, 5.8]
Week 32	120	71.49 (13.816)	68.90 [44.8, 113.4]	0.57 (1.783)	0.65 [-6.1, 7.3]

Parameter	Observed			Change from baseline	
Treatment Visit	n	Mean (SD)	Median [Min, Max]	Mean (SD)	Median [Min, Max]
Week 36	120	71.38 (13.699)	68.70 [44.2, 110.8]	0.46 (1.859)	0.45 [-4.7, 6.3]
Week 40	120	71.33 (13.894)	68.45 [43.4, 115.0]	0.40 (2.007)	0.35 [-8.2, 6.1]
Week 44	119	71.34 (13.777)	68.60 [43.8, 114.0]	0.45 (1.869)	0.30 [-4.8, 4.8]
Week 48	116	70.83 (13.579)	68.50 [43.4, 113.7]	0.40 (1.702)	0.35 [-4.4, 5.4]
Week 52	116	70.89 (13.554)	68.65 [43.9, 114.6]	0.46 (1.912)	0.25 [-4.4, 6.0]
LOCF Endpoint	127	70.92 (13.796)	68.50 [43.9, 114.6]	0.28 (2.077)	0.20 [-8.2, 6.0]
Imeglimin + GLIN (N = 64)					
Baseline	64	68.28 (13.850)	68.30 [43.3, 104.7]		
Week 4	64	68.19 (13.944)	67.20 [43.2, 103.8]	-0.09 (1.085)	0.10 [-4.2, 2.7]
Week 8	63	67.83 (13.878)	66.60 [43.0, 102.3]	-0.14 (1.332)	-0.10 [-4.6, 2.0]
Week 12	63	67.94 (13.937)	67.00 [43.0, 102.9]	-0.03 (1.683)	0.30 [-5.5, 3.7]
Week 16	63	68.00 (13.900)	67.20 [42.6, 102.5]	0.02 (2.136)	0.50 [-9.3, 4.7]
Week 20	62	67.83 (14.001)	67.30 [41.4, 101.9]	-0.03 (2.444)	0.50 [-12.1, 3.8]
Week 24	62	67.95 (13.904)	66.95 [42.2, 102.6]	0.09 (2.836)	0.60 [-15.2, 4.9]
Week 28	62	68.13 (13.881)	66.65 [42.7, 101.7]	0.27 (2.844)	0.80 [-16.5, 3.5]
Week 32	62	68.06 (13.692)	67.00 [43.9, 102.5]	0.20 (3.011)	0.50 [-18.0, 3.5]
Week 36	60	67.94 (14.075)	66.65 [43.9, 103.2]	0.18 (3.295)	0.70 [-19.7, 4.2]
Week 40	60	67.87 (13.805)	66.15 [44.1, 103.0]	0.11 (3.589)	0.80 [-22.0, 4.6]
Week 44	60	67.58 (13.773)	65.65 [43.6, 101.6]	-0.18 (3.832)	0.45 [-23.6, 4.7]
Week 48	60	67.56 (13.844)	66.20 [42.5, 101.5]	-0.20 (4.046)	0.45 [-25.9, 5.0]
Week 52	59	67.62 (13.718)	65.90 [42.5, 101.6]	-0.43 (4.169)	0.30 [-27.1, 3.7]
LOCF Endpoint	64	67.89 (13.593)	66.35 [42.5, 101.6]	-0.39 (4.025)	0.30 [-27.1, 3.7]
Imeglimin + BIG (N = 64)					
Baseline	64	72.25 (11.451)	72.30 [46.9, 99.1]		
Week 4	64	72.15 (11.515)	72.30 [46.5, 98.3]	-0.11 (0.997)	-0.35 [-2.0, 2.1]
Week 8	64	71.77 (11.635)	72.00 [46.0, 98.1]	-0.49 (1.113)	-0.55 [-3.3, 2.3]
Week 12	64	71.77 (11.816)	71.63 [46.2, 100.0]	-0.49 (1.447)	-0.58 [-4.7, 3.1]
Week 16	64	71.41 (11.920)	71.10 [45.5, 99.1]	-0.85 (1.660)	-0.85 [-5.4, 3.9]

Parameter	Observed			Change from baseline	
Treatment Visit	n	Mean (SD)	Median [Min, Max]	Mean (SD)	Median [Min, Max]
Week 20	63	71.50 (12.092)	70.80 [46.1, 101.0]	-0.74 (1.820)	-0.70 [-4.3, 3.1]
Week 24	63	71.54 (12.170)	69.90 [46.1, 99.7]	-0.70 (1.996)	-0.60 [-6.0, 3.7]
Week 28	61	72.04 (12.216)	72.10 [45.7, 98.5]	-0.64 (2.072)	-0.40 [-5.9, 4.2]
Week 32	60	71.78 (11.991)	71.30 [45.9, 98.4]	-0.74 (2.006)	-0.70 [-5.2, 3.3]
Week 36	60	72.12 (11.796)	71.40 [45.8, 98.7]	-0.40 (1.873)	0.10 [-5.0, 4.4]
Week 40	59	72.64 (11.508)	71.70 [45.9, 97.8]	-0.20 (1.947)	0.00 [-4.6, 5.0]
Week 44	59	72.66 (11.500)	72.40 [46.2, 96.4]	-0.18 (1.900)	0.10 [-4.3, 3.6]
Week 48	58	72.41 (11.430)	72.50 [45.7, 97.4]	-0.14 (1.795)	-0.10 [-4.4, 4.2]
Week 52	58	72.47 (11.686)	72.80 [46.1, 100.2]	-0.08 (1.911)	0.00 [-4.4, 4.6]
LOCF Endpoint	64	72.18 (11.944)	72.10 [46.1, 100.2]	-0.07 (1.956)	-0.15 [-4.4, 4.6]
Imeglimin + AGI (N = 64)					
Baseline	64	72.62 (16.757)	68.55 [46.6, 132.8]		
Week 4	64	72.83 (16.955)	69.10 [46.4, 133.2]	0.21 (0.764)	0.30 [-1.3, 1.9]
Week 8	64	72.61 (17.223)	69.55 [45.0, 134.0]	-0.02 (1.168)	0.05 [-2.7, 2.9]
Week 12	64	72.67 (17.273)	69.75 [44.4, 133.0]	0.05 (1.509)	0.05 [-5.9, 3.1]
Week 16	64	72.51 (17.314)	69.55 [43.7, 133.6]	-0.11 (1.783)	-0.15 [-7.4, 4.4]
Week 20	64	72.58 (17.361)	68.80 [44.2, 136.0]	-0.04 (1.936)	0.10 [-8.2, 3.9]
Week 24	63	72.56 (17.510)	68.80 [44.4, 134.0]	-0.05 (2.020)	0.20 [-6.9, 4.0]
Week 28	64	72.57 (17.550)	69.50 [44.1, 137.0]	-0.06 (2.374)	0.25 [-7.0, 5.6]
Week 32	62	72.43 (17.687)	69.05 [44.3, 137.4]	0.04 (2.302)	0.35 [-6.7, 5.0]
Week 36	62	72.59 (17.724)	69.10 [43.3, 136.2]	0.20 (2.504)	0.35 [-7.1, 5.2]
Week 40	62	72.45 (17.243)	69.10 [43.8, 134.6]	0.07 (2.561)	0.40 [-8.6, 4.6]
Week 44	62	72.41 (16.985)	69.35 [44.3, 134.4]	0.02 (2.654)	0.25 [-10.5, 5.2]
Week 48	62	72.01 (16.920)	69.05 [44.8, 133.2]	-0.38 (2.902)	-0.30 [-13.2, 4.1]
Week 52	62	71.78 (16.636)	69.25 [45.2, 132.2]	-0.60 (3.207)	-0.35 [-17.5, 4.9]
LOCF Endpoint	64	71.97 (16.469)	69.60 [45.2, 132.2]	-0.65 (3.184)	-0.40 [-17.5, 4.9]
Imeglimin + TZD (N = 65)					
Baseline	65	75.57 (16.133)	74.00 [44.2, 117.2]		

Parameter	Observed			Change from baseline	
Treatment Visit	n	Mean (SD)	Median [Min, Max]	Mean (SD)	Median [Min, Max]
Week 4	65	75.74 (16.499)	73.60 [42.0, 116.4]	0.17 (1.292)	0.20 [-4.3, 2.8]
Week 8	65	75.82 (16.608)	72.70 [43.8, 118.6]	0.25 (1.590)	0.30 [-4.2, 4.2]
Week 12	65	75.94 (16.776)	74.00 [45.0, 119.5]	0.36 (1.631)	0.50 [-3.4, 4.4]
Week 16	64	75.76 (16.604)	74.05 [45.4, 118.9]	0.45 (1.658)	0.55 [-3.4, 3.5]
Week 20	65	75.97 (16.515)	74.30 [45.2, 121.1]	0.40 (2.213)	0.30 [-11.0, 4.1]
Week 24	65	76.17 (16.639)	74.10 [45.0, 120.6]	0.60 (2.255)	0.60 [-10.3, 3.9]
Week 28	65	76.34 (16.519)	74.20 [45.4, 118.4]	0.76 (2.293)	0.70 [-8.1, 5.0]
Week 32	65	76.51 (16.829)	74.80 [45.8, 120.5]	0.93 (2.298)	1.00 [-6.8, 4.7]
Week 36	65	76.72 (16.964)	74.60 [46.4, 121.3]	1.14 (2.286)	1.10 [-4.5, 7.3]
Week 40	65	76.64 (16.843)	74.00 [46.8, 121.8]	1.06 (2.325)	1.00 [-5.6, 6.2]
Week 44	65	76.56 (16.987)	74.40 [46.4, 124.1]	0.99 (3.285)	1.00 [-14.1, 7.1]
Week 48	65	76.66 (16.919)	74.90 [46.4, 124.5]	1.08 (3.173)	1.60 [-13.3, 7.3]
Week 52	65	76.37 (16.781)	74.85 [46.8, 123.3]	0.79 (2.786)	0.90 [-10.1, 6.3]
LOCF Endpoint	65	76.37 (16.781)	74.85 [46.8, 123.3]	0.79 (2.786)	0.90 [-10.1, 6.3]
Imeglimin + DPP4-I (N = 63)					
Baseline	63	64.88 (12.882)	63.00 [45.4, 117.4]		
Week 4	63	64.67 (13.096)	63.30 [43.8, 118.0]	-0.21 (0.966)	-0.30 [-2.3, 2.4]
Week 8	62	64.43 (13.421)	63.10 [44.0, 120.1]	-0.29 (1.238)	-0.15 [-5.2, 2.7]
Week 12	62	64.23 (13.414)	62.45 [42.9, 118.0]	-0.49 (1.278)	-0.55 [-3.8, 2.6]
Week 16	62	64.38 (13.517)	62.95 [42.3, 118.2]	-0.34 (1.527)	-0.48 [-3.3, 2.5]
Week 20	61	64.56 (13.518)	63.10 [42.0, 117.8]	-0.23 (1.711)	-0.20 [-3.8, 3.6]
Week 24	61	64.74 (13.505)	62.50 [42.7, 118.7]	-0.05 (1.829)	-0.20 [-4.3, 4.0]
Week 28	59	64.82 (13.704)	62.80 [42.6, 117.8]	0.02 (1.755)	-0.10 [-3.5, 4.1]
Week 32	60	64.68 (13.296)	62.35 [42.3, 114.8]	-0.09 (1.997)	0.05 [-4.9, 4.3]
Week 36	60	64.68 (13.277)	62.65 [42.7, 115.8]	-0.09 (2.064)	-0.20 [-5.1, 4.9]
Week 40	60	64.89 (13.272)	62.60 [43.0, 115.6]	0.12 (1.932)	0.10 [-3.9, 4.8]
Week 44	60	64.92 (13.278)	62.50 [42.6, 116.0]	0.15 (1.750)	0.05 [-4.0, 4.8]

Parameter	Observed			Change from baseline	
Treatment Visit	n	Mean (SD)	Median [Min, Max]	Mean (SD)	Median [Min, Max]
Week 48	60	64.77 (13.252)	63.05 [43.3, 116.6]	0.00 (1.837)	-0.08 [-4.3, 5.0]
Week 52	60	64.76 (13.244)	62.65 [42.4, 117.3]	-0.01 (1.809)	0.10 [-4.3, 5.4]
LOCF Endpoint	63	64.82 (13.005)	62.40 [42.4, 117.3]	-0.07 (1.832)	0.10 [-4.3, 5.4]
Imeglimin + GLP1-RA (N = 70)					
Baseline	70	70.85 (15.130)	72.60 [39.0, 119.2]		
Week 4	70	70.98 (15.199)	72.30 [38.0, 120.2]	0.13 (0.817)	0.10 [-1.5, 1.8]
Week 8	69	71.00 (15.252)	72.20 [38.8, 121.2]	-0.10 (1.345)	-0.10 [-4.5, 4.1]
Week 12	68	71.13 (15.147)	73.05 [38.7, 121.8]	-0.18 (1.631)	-0.30 [-4.7, 5.3]
Week 16	69	70.74 (15.207)	71.70 [38.5, 121.2]	-0.36 (2.018)	-0.50 [-5.3, 7.4]
Week 20	69	70.86 (14.963)	71.80 [39.5, 119.8]	-0.24 (2.185)	-0.30 [-5.7, 6.8]
Week 24	69	71.05 (15.020)	73.40 [38.6, 121.0]	-0.04 (2.289)	-0.20 [-5.7, 6.1]
Week 28	69	71.15 (15.096)	73.30 [37.3, 119.6]	0.06 (2.359)	-0.30 [-5.6, 6.8]
Week 32	69	70.89 (15.039)	72.80 [39.4, 122.0]	-0.21 (2.145)	-0.20 [-6.2, 5.5]
Week 36	69	71.00 (15.102)	73.10 [39.2, 121.2]	-0.10 (2.326)	-0.10 [-7.7, 6.1]
Week 40	69	70.98 (15.158)	73.70 [40.2, 121.2]	-0.11 (2.472)	0.00 [-6.9, 4.8]
Week 44	67	71.00 (14.999)	72.60 [39.9, 120.8]	-0.19 (2.519)	0.20 [-7.5, 5.9]
Week 48	66	71.03 (15.006)	73.05 [40.3, 120.0]	-0.24 (2.427)	0.05 [-7.8, 4.9]
Week 52	67	70.85 (14.949)	72.00 [39.9, 119.0]	-0.34 (2.378)	-0.40 [-7.5, 4.6]
LOCF Endpoint	70	70.55 (14.918)	71.60 [39.9, 119.0]	-0.30 (2.356)	-0.35 [-7.5, 4.6]
Imeglimin + SGLT2-I (N = 63)					
Baseline	63	72.76 (16.512)	70.70 [41.2, 129.8]		
Week 4	63	72.87 (16.664)	71.30 [40.9, 130.4]	0.11 (0.768)	0.10 [-2.3, 2.2]
Week 8	63	72.90 (16.424)	70.90 [41.7, 127.8]	0.15 (1.153)	0.10 [-4.3, 2.8]
Week 12	63	72.89 (16.497)	70.30 [41.8, 128.0]	0.13 (1.329)	0.10 [-3.7, 3.6]
Week 16	63	72.90 (16.560)	70.50 [42.3, 129.8]	0.14 (1.772)	0.40 [-6.3, 4.6]
Week 20	63	72.80 (16.433)	71.00 [41.6, 130.8]	0.04 (1.839)	0.40 [-8.4, 4.7]
Week 24	63	73.02 (16.532)	71.10 [41.5, 132.4]	0.26 (1.578)	0.30 [-5.9, 4.0]
Week 28	63	73.05 (16.553)	71.40 [40.8, 132.0]	0.29 (1.680)	0.40 [-7.7, 3.4]

Parameter	Observed			Change from baseline	
Treatment Visit	n	Mean (SD)	Median [Min, Max]	Mean (SD)	Median [Min, Max]
Week 32	63	73.13 (16.438)	71.50 [39.4, 128.0]	0.37 (1.807)	0.40 [-6.9, 4.6]
Week 36	63	73.02 (16.065)	71.40 [40.4, 126.6]	0.27 (1.955)	0.40 [-7.8, 4.8]
Week 40	63	73.18 (16.355)	71.70 [41.6, 128.0]	0.42 (1.691)	0.40 [-3.0, 4.1]
Week 44	62	73.45 (16.057)	72.65 [41.7, 128.6]	0.38 (2.096)	0.45 [-7.3, 6.7]
Week 48	63	72.68 (16.321)	72.10 [41.3, 129.8]	-0.08 (1.983)	0.10 [-5.9, 4.3]
Week 52	62	73.03 (16.148)	71.50 [41.3, 129.2]	-0.04 (1.973)	0.15 [-7.5, 3.9]
LOCF Endpoint	63	72.66 (16.278)	71.50 [41.3, 129.2]	-0.10 (2.008)	0.10 [-7.5, 3.9]

- Abbreviations: SD, standard deviation; LOCF, Last Observation Carried Forward; SU, Sulphonylurea; GLIN, Glinide; BIG, Biguanide; AGI, Alpha glucosidase inhibitor; TZD, Thiazolidinedione; DPP4-I, Dipeptidyl peptidase-4 inhibitor; GLP1-RA, Glucagon-like peptide 1 receptor agonist; SGLT2-I, Sodium glucose cotransporter 2 inhibitor
- "Imeglimin" in this table means "Imeglimin 1000 mg twice daily".

Control No:<<t-s-103-vsign-019lt.sas, 2020-03-06T00:09:38>>

Table S-105 Summary of Change from Baseline in eGFR (mL/min/1.73m2) to Week 16 in 16-Week Double-blind Period in Combination with Insulin Therapy (PXL008-020; Safety Population)

Parameter	Observed			Change from baseline	
Treatment Visit	n	Mean (SD)	Median [Min, Max]	Mean (SD)	Median [Min, Max]
eGFR (mL/min/1.73m2)					
Placebo + Insulin (N = 107)					
Baseline	107	77.3683 (13.72944)	75.7270 [60.249, 138.012]		
Week 16	104	76.6415 (12.33916)	75.6915 [54.517, 117.683]	-0.9302 (8.59072)	-0.2915 [-24.956, 18.237]
LOCF Endpoint	104	76.6415 (12.33916)	75.6915 [54.517, 117.683]	-0.9302 (8.59072)	-0.2915 [-24.956, 18.237]
Imeglimin 1000 mg bid + Insulin (N = 108)					
Baseline	108	77.0865 (12.31103)	75.3615 [60.196, 129.390]		
Week 16	108	76.9870 (14.46085)	73.7635 [53.975, 135.519]	-0.0995 (10.04149)	-0.3070 [-31.776, 32.247]
LOCF Endpoint	108	76.9870 (14.46085)	73.7635 [53.975, 135.519]	-0.0995 (10.04149)	-0.3070 [-31.776, 32.247]

- Abbreviations: bid, Twice a day; SD, standard deviation; LOCF, Last Observation Carried Forward; eGFR, Estimated Glomerular Filtration Rate

Control No:<<t-s-105-labot-020db.sas, 2020-03-06T00:12:16>>

Table S-107 Summary of Change from Baseline in Weight (kg) at All Visits in 16-Week Double-blind Period in Combination with Insulin Therapy (PXL008-020; Safety Population)

Parameter	Observed			Change from baseline	
Treatment Visit	n	Mean (SD)	Median [Min, Max]	Mean (SD)	Median [Min, Max]
Weight (kg)					
Placebo + Insulin (N = 107)					
Baseline	107	67.54 (11.816)	66.90 [44.2, 106.2]		
Week 4	106	67.21 (11.395)	67.70 [44.2, 105.0]	-0.01 (0.926)	0.00 [-3.0, 5.4]
Week 8	105	67.02 (11.364)	66.90 [43.9, 104.8]	-0.22 (0.922)	-0.30 [-2.8, 2.5]
Week 12	104	67.04 (11.443)	67.00 [43.8, 104.0]	-0.20 (1.233)	-0.10 [-3.7, 2.6]
Week 16	104	67.02 (11.406)	66.50 [43.4, 102.9]	-0.23 (1.393)	-0.10 [-5.3, 2.9]
LOCF Endpoint	106	67.05 (11.301)	66.75 [43.4, 102.9]	-0.18 (1.484)	-0.10 [-5.3, 5.4]
Imeglimin 1000 mg bid + Insulin (N = 108)					
Baseline	108	67.13 (12.266)	65.40 [41.8, 104.1]		
Week 4	108	67.31 (12.346)	65.75 [40.5, 105.5]	0.18 (0.861)	0.30 [-3.0, 3.0]
Week 8	108	67.42 (12.522)	65.55 [40.7, 105.1]	0.29 (1.163)	0.50 [-3.5, 2.8]
Week 12	108	67.59 (12.486)	66.60 [41.0, 105.2]	0.46 (1.253)	0.50 [-4.4, 3.0]
Week 16	108	67.61 (12.334)	66.55 [41.2, 104.1]	0.48 (1.472)	0.70 [-5.9, 3.7]
LOCF Endpoint	108	67.61 (12.334)	66.55 [41.2, 104.1]	0.48 (1.472)	0.70 [-5.9, 3.7]

- Abbreviations: bid, Twice a day; SD, standard deviation; LOCF, Last Observation Carried Forward

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Table S-109 Summary of Change from Baseline in eGFR (mL/min/1.73m2) to Week 52 in 52-Week Long-term Period in Combination with Insulin Therapy (PXL008-020; Long-term Safety Population)

Parameter	Observed			Change from baseline	
Treatment Visit	n	Mean (SD)	Median [Min, Max]	Mean (SD)	Median [Min, Max]
eGFR (mL/min/1.73m2)					
Placebo/Imeglimin + Insulin (N = 101)					
Baseline	101	76.4253 (12.27761)	75.6560 [54.517, 117.683]		
Week 20	99	75.6322 (12.96706)	74.3700 [52.984, 117.683]	-0.9534 (8.56335)	0.0000 [-17.545, 18.006]
Week 36	98	74.6340 (12.03214)	74.8670 [54.517, 112.360]	-1.8655 (9.34129)	-0.3060 [-31.776, 20.329]
LOCF Endpoint	99	74.8967 (12.25252)	75.0010 [54.517, 112.360]	-1.6889 (9.45815)	-0.3030 [-31.776, 20.329]
Imeglimin/Imeglimin + Insulin (N = 108)					
Baseline	108	77.0865 (12.31103)	75.3615 [60.196, 129.390]		
Week 16	108	76.9870 (14.46085)	73.7635 [53.975, 135.519]	-0.0995 (10.04149)	-0.3070 [-31.776, 32.247]
Week 36	107	77.3757 (14.40255)	75.7540 [53.846, 128.610]	0.1603 (9.44814)	-0.2760 [-20.612, 29.804]
Week 52	107	75.8144 (14.50531)	74.3700 [48.841, 134.562]	-1.4009 (9.94208)	-0.3910 [-32.382, 28.397]
LOCF Endpoint	108	75.6963 (14.48948)	74.2170 [48.841, 134.562]	-1.3902 (9.89614)	-0.3910 [-32.382, 28.397]
Imeglimin + Insulin Total (N = 209)					
Baseline	209	76.7669 (12.26977)	75.6560 [54.517, 129.390]		
Week 16	108	76.9870 (14.46085)	73.7635 [53.975, 135.519]	-0.0995 (10.04149)	-0.3070 [-31.776, 32.247]
Week 20	99	75.6322 (12.96706)	74.3700 [52.984, 117.683]	-0.9534 (8.56335)	0.0000 [-17.545, 18.006]
Week 36	205	76.0650 (13.36064)	75.3250 [53.846, 128.610]	-0.8081 (9.42890)	-0.2850 [-31.776, 29.804]
Week 52	107	75.8144 (14.50531)	74.3700 [48.841, 134.562]	-1.4009 (9.94208)	-0.3910 [-32.382, 28.397]
LOCF Endpoint	207	75.3139 (13.43979)	74.7330 [48.841, 134.562]	-1.5331 (9.66684)	-0.3540 [-32.382, 28.397]

- Abbreviations: SD, standard deviation; LOCF, Last Observation Carried Forward; eGFR, Estimated Glomerular Filtration Rate
- "Imeglimin" in this table means "Imeglimin 1000 mg twice daily".
- The Long-term Safety Population excludes data during administration of placebo in the double-blind period.
- "Imeglimin + Insulin Total" is the sum of subjects in the placebo group in the open-label period and Imeglimin group in the double-blind and open-label periods.
- For "Placebo/Imeglimin + Insulin" group, baseline was defined as last visit with non-missing value prior to or at the day of first dose of Investigational Medicinal Product (IMP) in open-label treatment period. For "Imeglimin/Imeglimin + Insulin" group, baseline was the same as for the double-blind treatment period.

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Table S-111 Summary of Change from Baseline in Weight (kg) at All Visits in 52-Week Long-term Period in Combination with Insulin Therapy (PXL008-020; Long-term Safety Population)

Parameter	Observed			Change from baseline	
Treatment Visit	n	Mean (SD)	Median [Min, Max]	Mean (SD)	Median [Min, Max]
Weight (kg)					
Placebo/Imeglimin + Insulin (N = 101)					
Baseline	101	66.65 (10.991)	66.30 [43.4, 97.8]		
Week 4	101	66.92 (10.907)	67.30 [43.7, 99.6]	0.27 (0.798)	0.20 [-2.0, 2.7]
Week 8	101	67.04 (11.219)	66.60 [44.0, 100.8]	0.39 (1.074)	0.30 [-2.6, 3.2]
Week 12	101	67.18 (11.232)	67.20 [42.9, 100.7]	0.53 (1.149)	0.50 [-2.3, 3.3]
Week 16	99	67.45 (11.422)	67.50 [43.2, 99.6]	0.69 (1.345)	0.60 [-2.4, 6.0]
Week 20	99	67.51 (11.567)	67.70 [43.4, 98.9]	0.75 (1.560)	0.80 [-3.0, 6.3]
Week 24	99	67.52 (11.596)	67.80 [43.4, 99.9]	0.76 (1.579)	0.60 [-2.7, 6.4]
Week 28	98	67.50 (11.789)	67.40 [43.1, 100.9]	0.78 (1.617)	0.70 [-2.6, 6.7]
Week 32	98	67.33 (11.727)	68.05 [43.7, 101.8]	0.56 (1.838)	0.50 [-3.4, 5.9]
Week 36	98	67.32 (11.783)	67.70 [43.4, 102.4]	0.56 (1.823)	0.50 [-3.6, 5.8]
LOCF Endpoint	101	67.19 (11.651)	67.20 [43.4, 102.4]	0.54 (1.804)	0.50 [-3.6, 5.8]
Imeglimin/Imeglimin + Insulin (N = 108)					
Baseline	108	67.13 (12.266)	65.40 [41.8, 104.1]		
Week 4	108	67.31 (12.346)	65.75 [40.5, 105.5]	0.18 (0.861)	0.30 [-3.0, 3.0]
Week 8	108	67.42 (12.522)	65.55 [40.7, 105.1]	0.29 (1.163)	0.50 [-3.5, 2.8]
Week 12	108	67.59 (12.486)	66.60 [41.0, 105.2]	0.46 (1.253)	0.50 [-4.4, 3.0]
Week 16	108	67.61 (12.334)	66.55 [41.2, 104.1]	0.48 (1.472)	0.70 [-5.9, 3.7]
Week 20	108	67.75 (12.443)	67.15 [41.6, 105.5]	0.62 (1.747)	0.80 [-7.0, 4.0]
Week 24	108	67.82 (12.392)	66.95 [41.6, 104.4]	0.69 (1.810)	0.90 [-6.1, 4.5]
Week 28	108	67.91 (12.401)	66.70 [41.5, 104.4]	0.78 (1.889)	0.90 [-7.5, 5.5]
Week 32	108	67.87 (12.280)	66.95 [42.2, 104.4]	0.74 (2.071)	0.80 [-8.6, 6.4]
Week 36	108	67.91 (12.161)	66.55 [41.5, 101.2]	0.78 (2.074)	1.00 [-8.2, 6.5]
Week 40	107	67.91 (12.188)	66.60 [41.9, 102.3]	0.73 (2.176)	1.10 [-7.6, 5.0]
Week 44	107	67.73 (12.076)	67.40 [41.5, 102.7]	0.55 (2.234)	0.80 [-6.6, 5.4]

Parameter	Observed			Change from baseline	
Treatment Visit	n	Mean (SD)	Median [Min, Max]	Mean (SD)	Median [Min, Max]
Week 48	107	67.80 (12.261)	66.90 [41.4, 103.3]	0.61 (2.297)	0.70 [-7.2, 7.6]
Week 52	107	67.82 (12.183)	67.30 [41.7, 101.9]	0.64 (2.401)	0.90 [-6.1, 8.2]
LOCF Endpoint	108	67.79 (12.131)	67.15 [41.7, 101.9]	0.66 (2.399)	0.90 [-6.1, 8.2]
Imeglimin + Insulin Total (N = 209)					
Baseline	209	66.90 (11.642)	66.10 [41.8, 104.1]		
Week 4	209	67.12 (11.647)	67.20 [40.5, 105.5]	0.22 (0.830)	0.30 [-3.0, 3.0]
Week 8	209	67.24 (11.883)	66.50 [40.7, 105.1]	0.34 (1.120)	0.40 [-3.5, 3.2]
Week 12	209	67.39 (11.870)	67.20 [41.0, 105.2]	0.49 (1.202)	0.50 [-4.4, 3.3]
Week 16	207	67.53 (11.878)	67.00 [41.2, 104.1]	0.58 (1.414)	0.70 [-5.9, 6.0]
Week 20	207	67.63 (12.003)	67.60 [41.6, 105.5]	0.68 (1.657)	0.80 [-7.0, 6.3]
Week 24	207	67.68 (11.990)	67.10 [41.6, 104.4]	0.72 (1.700)	0.60 [-6.1, 6.4]
Week 28	206	67.72 (12.086)	67.25 [41.5, 104.4]	0.78 (1.761)	0.80 [-7.5, 6.7]
Week 32	206	67.61 (11.994)	67.65 [42.2, 104.4]	0.65 (1.961)	0.60 [-8.6, 6.4]
Week 36	206	67.63 (11.957)	67.30 [41.5, 102.4]	0.68 (1.957)	0.80 [-8.2, 6.5]
Week 40	107	67.91 (12.188)	66.60 [41.9, 102.3]	0.73 (2.176)	1.10 [-7.6, 5.0]
Week 44	107	67.73 (12.076)	67.40 [41.5, 102.7]	0.55 (2.234)	0.80 [-6.6, 5.4]
Week 48	107	67.80 (12.261)	66.90 [41.4, 103.3]	0.61 (2.297)	0.70 [-7.2, 7.6]
Week 52	107	67.82 (12.183)	67.30 [41.7, 101.9]	0.64 (2.401)	0.90 [-6.1, 8.2]
LOCF Endpoint	209	67.50 (11.876)	67.20 [41.7, 102.4]	0.60 (2.128)	0.60 [-6.1, 8.2]

- Abbreviations: SD, standard deviation; LOCF, Last Observation Carried Forward
- "Imeglimin" in this table means "Imeglimin 1000 mg twice daily".
- The Long-term Safety Population excludes data during administration of placebo in the double-blind period.
- "Imeglimin + Insulin Total" is the sum of subjects in the placebo group in the open-label period and Imeglimin group in the double-blind and open-label periods.
- For "Placebo/Imeglimin + Insulin" group, baseline was defined as last visit with non-missing value prior to or at the day of first dose of Investigational Medicinal Product (IMP) in open-label treatment period. For "Imeglimin/Imeglimin + Insulin" group, baseline was the same as for the double-blind treatment period.

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Table S-160 Summary of Treatment Emergent Adverse Events by System Organ Class and Preferred Term in All Patients Treated Imeglimin (PXL008-014, PXL008-018, PXL008-019, PXL008-020; Safety Population, Long-term Safety Population)

				Imeglimin 1000 mg bid N = 1103		Imeglimin All N = 1253	
System Organ Class	器官別大分類	Preferred Term	基本語	AE n (%)	Serious AE n (%)	AE n (%)	Serious AE n (%)
Any TEAE	全事象	(Total)	（計）	801 (72.6%)	60 (5.4%)	907 (72.4%)	61 (4.9%)
Infections and infestations	感染症および寄生虫症	(Total)	（計）	443 (40.2%)	5 (0.5%)	496 (39.6%)	5 (0.4%)
		Nasopharyngitis	上咽頭炎	289 (26.2%)	0	327 (26.1%)	0
		Influenza	インフルエンザ	40 (3.6%)	0	41 (3.3%)	0
		Pharyngitis	咽頭炎	36 (3.3%)	0	37 (3.0%)	0
		Bronchitis	気管支炎	25 (2.3%)	0	29 (2.3%)	0
		Gastroenteritis	胃腸炎	21 (1.9%)	0	23 (1.8%)	0
		Periodontitis	歯周炎	16 (1.5%)	0	18 (1.4%)	0
		Cystitis	膀胱炎	15 (1.4%)	0	17 (1.4%)	0
		Herpes zoster	帯状疱疹	12 (1.1%)	0	13 (1.0%)	0
		Conjunctivitis	結膜炎	9 (0.8%)	0	9 (0.7%)	0
		Upper respiratory tract infection	上気道感染	8 (0.7%)	0	9 (0.7%)	0
		Urinary tract infection	尿路感染	7 (0.6%)	0	7 (0.6%)	0
		Otitis externa	外耳炎	5 (0.5%)	0	6 (0.5%)	0
		Tinea pedis	足部白癬	6 (0.5%)	0	6 (0.5%)	0
		Gingivitis	歯肉炎	5 (0.5%)	0	5 (0.4%)	0
		Pericoronitis	歯冠周囲炎	4 (0.4%)	0	5 (0.4%)	0

System Organ Class	器官別大分類	Preferred Term	基本語	Imeglimin 1000 mg bid N = 1103 AE n (%)	Imeglimin 1000 mg bid N = 1103 Serious AE n (%)	Imeglimin All N = 1253 AE n (%)	Imeglimin All N = 1253 Serious AE n (%)
		Pneumonia	肺炎	5 (0.5%)	1 (<0.1%)	5 (0.4%)	1 (<0.1%)
		Asymptomatic bacteriuria	無症候性細菌尿	4 (0.4%)	0	4 (0.3%)	0
		Folliculitis	毛包炎	4 (0.4%)	0	4 (0.3%)	0
		Gastroenteritis viral	ウイルス性胃腸炎	3 (0.3%)	0	4 (0.3%)	0
		Oral herpes	口腔ヘルペス	4 (0.4%)	0	4 (0.3%)	0
		Sinusitis	副鼻腔炎	4 (0.4%)	0	4 (0.3%)	0
		Dermatophytosis of nail	爪の皮膚糸状菌症	3 (0.3%)	0	3 (0.2%)	0
		Helicobacter infection	ヘリコバクター感染	3 (0.3%)	0	3 (0.2%)	0
		Hordeolum	麦粒腫	3 (0.3%)	0	3 (0.2%)	0
		Otitis media acute	急性中耳炎	3 (0.3%)	0	3 (0.2%)	0
		Pulpitis dental	歯髄炎	2 (0.2%)	0	3 (0.2%)	0
		Rhinitis	鼻炎	3 (0.3%)	0	3 (0.2%)	0
		Appendicitis	虫垂炎	2 (0.2%)	2 (0.2%)	2 (0.2%)	2 (0.2%)
		Chronic sinusitis	慢性副鼻腔炎	2 (0.2%)	0	2 (0.2%)	0
		Diverticulitis	憩室炎	2 (0.2%)	0	2 (0.2%)	0
		Enteritis infectious	感染性腸炎	2 (0.2%)	0	2 (0.2%)	0
		Furuncle	せつ	2 (0.2%)	0	2 (0.2%)	0
		Impetigo	膿痂疹	2 (0.2%)	0	2 (0.2%)	0
		Otitis media	中耳炎	2 (0.2%)	0	2 (0.2%)	0
		Paronychia	爪囲炎	2 (0.2%)	0	2 (0.2%)	0

System Organ Class	器官別大分類	Preferred Term	基本語	Imeglimin 1000 mg bid N = 1103 AE n (%)	Imeglimin 1000 mg bid N = 1103 Serious AE n (%)	Imeglimin All N = 1253 AE n (%)	Imeglimin All N = 1253 Serious AE n (%)
		Pneumonia bacterial	細菌性肺炎	2 (0.2%)	1 (<0.1%)	2 (0.2%)	1 (<0.1%)
		Acute sinusitis	急性副鼻腔炎	1 (<0.1%)	0	1 (<0.1%)	0
		Bacterial vulvovaginitis	細菌性外陰腟炎	1 (<0.1%)	0	1 (<0.1%)	0
		Bronchitis bacterial	細菌性気管支炎	1 (<0.1%)	0	1 (<0.1%)	0
		Cellulitis	蜂巣炎	1 (<0.1%)	0	1 (<0.1%)	0
		Conjunctivitis bacterial	細菌性結膜炎	0	0	1 (<0.1%)	0
		Eczema impetiginous	膿痂疹性湿疹	1 (<0.1%)	0	1 (<0.1%)	0
		Endometritis	子宮内膜炎	1 (<0.1%)	0	1 (<0.1%)	0
		Enterocolitis viral	ウイルス性腸炎	1 (<0.1%)	0	1 (<0.1%)	0
		Erysipelas	丹毒	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)
		Herpes simplex	単純ヘルペス	1 (<0.1%)	0	1 (<0.1%)	0
		Infected dermal cyst	感染性皮膚嚢腫	1 (<0.1%)	0	1 (<0.1%)	0
		Nasal vestibulitis	鼻前庭炎	1 (<0.1%)	0	1 (<0.1%)	0
		Parotitis	耳下腺炎	0	0	1 (<0.1%)	0
		Pneumonia mycoplasmal	マイコプラズマ性肺炎	1 (<0.1%)	0	1 (<0.1%)	0
		Skin bacterial infection	皮膚細菌感染	1 (<0.1%)	0	1 (<0.1%)	0
		Skin infection	皮膚感染	1 (<0.1%)	0	1 (<0.1%)	0
		Soft tissue infection	軟部組織感染	1 (<0.1%)	0	1 (<0.1%)	0
		Streptococcal infection	レンサ球菌感染	1 (<0.1%)	0	1 (<0.1%)	0
		Subcutaneous abscess	皮下組織膿瘍	1 (<0.1%)	0	1 (<0.1%)	0

System Organ Class	器官別大分類	Preferred Term	基本語	Imeglimin 1000 mg bid N = 1103 AE n (%)	Imeglimin 1000 mg bid N = 1103 Serious AE n (%)	Imeglimin All N = 1253 AE n (%)	Imeglimin All N = 1253 Serious AE n (%)
		Tinea infection	白癬感染	1 (<0.1%)	0	1 (<0.1%)	0
		Tonsillitis	扁桃炎	1 (<0.1%)	0	1 (<0.1%)	0
		Vaginal infection	腟感染	1 (<0.1%)	0	1 (<0.1%)	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	(Total)	（計）	22 (2.0%)	13 (1.2%)	23 (1.8%)	14 (1.1%)
		Papillary thyroid cancer	乳頭様甲状腺癌	2 (0.2%)	2 (0.2%)	2 (0.2%)	2 (0.2%)
		Uterine leiomyoma	子宮平滑筋腫	2 (0.2%)	1 (<0.1%)	2 (0.2%)	1 (<0.1%)
		Benign neoplasm of spinal cord	脊髄の良性新生物	1 (<0.1%)	0	1 (<0.1%)	0
		Benign neoplasm of thyroid gland	甲状腺の良性新生物	1 (<0.1%)	0	1 (<0.1%)	0
		Bladder cancer	膀胱癌	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)
		Cholangiocarcinoma	胆管細胞癌	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)
		Colon adenoma	大腸腺腫	1 (<0.1%)	0	1 (<0.1%)	0
		Colon cancer stage I	結腸癌第 1 期	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)
		Endometrial cancer stage III	子宮内膜癌第 3 期	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)
		Haemangioma of liver	肝臓血管腫	1 (<0.1%)	0	1 (<0.1%)	0
		Intraductal papillary mucinous neoplasm	膵管内乳頭粘液性腫瘍	1 (<0.1%)	0	1 (<0.1%)	0
		Invasive ductal breast carcinoma	浸潤性乳管癌	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)

System Organ Class	器官別大分類	Preferred Term	基本語	Imeglimin 1000 mg bid N = 1103 AE n (%)	Imeglimin 1000 mg bid N = 1103 Serious AE n (%)	Imeglimin All N = 1253 AE n (%)	Imeglimin All N = 1253 Serious AE n (%)
		Lipoma	脂肪腫	1 (<0.1%)	0	1 (<0.1%)	0
		Pancreatic carcinoma	膵癌	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)
		Pancreatic carcinoma metastatic	遠隔転移を伴う膵癌	0	0	1 (<0.1%)	1 (<0.1%)
		Prostate cancer	前立腺癌	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)
		Rectal cancer	直腸癌	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)
		Seborrhoeic keratosis	脂漏性角化症	1 (<0.1%)	0	1 (<0.1%)	0
		Skin papilloma	皮膚乳頭腫	1 (<0.1%)	0	1 (<0.1%)	0
		Solid pseudopapillary tumour of the pancreas	膵の充実性偽乳頭状腫瘍	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)
		Testis cancer	精巣癌	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)
		Thyroid neoplasm	甲状腺新生物	1 (<0.1%)	0	1 (<0.1%)	0
Blood and lymphatic system disorders	血液およびリンパ系障害	(Total)	（計）	10 (0.9%)	0	10 (0.8%)	0
		Anaemia	貧血	3 (0.3%)	0	3 (0.2%)	0
		Lymphadenitis	リンパ節炎	2 (0.2%)	0	2 (0.2%)	0
		Anaemia macrocytic	大球性貧血	1 (<0.1%)	0	1 (<0.1%)	0
		Anaemia megaloblastic	巨赤芽球性貧血	1 (<0.1%)	0	1 (<0.1%)	0
		Iron deficiency anaemia	鉄欠乏性貧血	1 (<0.1%)	0	1 (<0.1%)	0
		Lymphadenopathy	リンパ節症	1 (<0.1%)	0	1 (<0.1%)	0
		Normocytic anaemia	正球性貧血	1 (<0.1%)	0	1 (<0.1%)	0

System Organ Class	器官別大分類	Preferred Term	基本語	Imeglimin 1000 mg bid N = 1103 AE n (%)	Imeglimin 1000 mg bid N = 1103 Serious AE n (%)	Imeglimin All N = 1253 AE n (%)	Imeglimin All N = 1253 Serious AE n (%)
Immune system disorders	免疫系障害	(Total)	（計）	14 (1.3%)	0	14 (1.1%)	0
		Seasonal allergy	季節性アレルギー	11 (1.0%)	0	11 (0.9%)	0
		Allergy to arthropod sting	節足動物刺傷アレルギー	2 (0.2%)	0	2 (0.2%)	0
		Food allergy	食物アレルギー	1 (<0.1%)	0	1 (<0.1%)	0
Endocrine disorders	内分泌障害	(Total)	（計）	3 (0.3%)	0	4 (0.3%)	0
		Autoimmune thyroiditis	自己免疫性甲状腺炎	1 (<0.1%)	0	1 (<0.1%)	0
		Hypothyroidism	甲状腺機能低下症	1 (<0.1%)	0	1 (<0.1%)	0
		Inappropriate antidiuretic hormone secretion	抗利尿ホルモン不適合分泌	1 (<0.1%)	0	1 (<0.1%)	0
		Thyroid cyst	甲状腺嚢腫	0	0	1 (<0.1%)	0
		Thyroid mass	甲状腺腫瘤	0	0	1 (<0.1%)	0
Metabolism and nutrition disorders	代謝および栄養障害	(Total)	（計）	183 (16.6%)	0	196 (15.6%)	0
		Hypoglycaemia	低血糖	136 (12.3%)	0	145 (11.6%)	0
		Hyperglycaemia	高血糖	28 (2.5%)	0	32 (2.6%)	0
		Decreased appetite	食欲減退	13 (1.2%)	0	13 (1.0%)	0
		Dyslipidaemia	脂質異常症	5 (0.5%)	0	5 (0.4%)	0
		Hyperuricaemia	高尿酸血症	4 (0.4%)	0	4 (0.3%)	0

System Organ Class	器官別大分類	Preferred Term	基本語	Imeglimin 1000 mg bid N = 1103 AE n (%)	Imeglimin 1000 mg bid N = 1103 Serious AE n (%)	Imeglimin All N = 1253 AE n (%)	Imeglimin All N = 1253 Serious AE n (%)
		Dehydration	脱水	1 (<0.1%)	0	1 (<0.1%)	0
		Gout	痛風	1 (<0.1%)	0	1 (<0.1%)	0
		Hyponatraemia	低ナトリウム血症	1 (<0.1%)	0	1 (<0.1%)	0
Psychiatric disorders	精神障害	(Total)	（計）	17 (1.5%)	0	19 (1.5%)	0
		Insomnia	不眠症	12 (1.1%)	0	14 (1.1%)	0
		Apathy	無感情	1 (<0.1%)	0	1 (<0.1%)	0
		Depressed mood	抑うつ気分	1 (<0.1%)	0	1 (<0.1%)	0
		Depression	うつ病	1 (<0.1%)	0	1 (<0.1%)	0
		Depressive symptom	抑うつ症状	1 (<0.1%)	0	1 (<0.1%)	0
		Mental fatigue	精神疲労	1 (<0.1%)	0	1 (<0.1%)	0
		Stress	ストレス	1 (<0.1%)	0	1 (<0.1%)	0
Nervous system disorders	神経系障害	(Total)	（計）	61 (5.5%)	5 (0.5%)	68 (5.4%)	5 (0.4%)
		Headache	頭痛	15 (1.4%)	0	17 (1.4%)	0
		Dizziness	浮動性めまい	6 (0.5%)	0	7 (0.6%)	0
		Diabetic neuropathy	糖尿病性ニューロパチー	6 (0.5%)	0	6 (0.5%)	0
		Carotid arteriosclerosis	頚動脈硬化症	4 (0.4%)	0	4 (0.3%)	0
		Carpal tunnel syndrome	手根管症候群	3 (0.3%)	0	3 (0.2%)	0
		Cervicobrachial syndrome	頚腕症候群	3 (0.3%)	0	3 (0.2%)	0

System Organ Class	器官別大分類	Preferred Term	基本語	Imeglimin 1000 mg bid N = 1103 AE n (%)	Imeglimin 1000 mg bid N = 1103 Serious AE n (%)	Imeglimin All N = 1253 AE n (%)	Imeglimin All N = 1253 Serious AE n (%)
		Intercostal neuralgia	肋間神経痛	3 (0.3%)	0	3 (0.2%)	0
		Loss of consciousness	意識消失	3 (0.3%)	0	3 (0.2%)	0
		Presyncope	失神寸前の状態	3 (0.3%)	0	3 (0.2%)	0
		Sciatica	坐骨神経痛	3 (0.3%)	1 (<0.1%)	3 (0.2%)	1 (<0.1%)
		Syncope	失神	2 (0.2%)	0	2 (0.2%)	0
		Autonomic nervous system imbalance	自律神経失調	1 (<0.1%)	0	1 (<0.1%)	0
		Carotid artery stenosis	頚動脈狭窄	1 (<0.1%)	0	1 (<0.1%)	0
		Cerebral infarction	脳梗塞	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)
		Cervical radiculopathy	頚髄神経根障害	1 (<0.1%)	0	1 (<0.1%)	0
		Dizziness postural	体位性めまい	0	0	1 (<0.1%)	0
		Dysaesthesia	異常感覚	1 (<0.1%)	0	1 (<0.1%)	0
		Dysgeusia	味覚異常	0	0	1 (<0.1%)	0
		Epilepsy	てんかん	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)
		Facial paralysis	顔面麻痺	1 (<0.1%)	0	1 (<0.1%)	0
		Hypoaesthesia	感覚鈍麻	1 (<0.1%)	0	1 (<0.1%)	0
		IVth nerve disorder	第４脳神経障害	0	0	1 (<0.1%)	0
		Lacunar infarction	ラクナ梗塞	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)
		Orthostatic intolerance	起立不耐性	0	0	1 (<0.1%)	0
		Paraesthesia	錯感覚	1 (<0.1%)	0	1 (<0.1%)	0
		Post herpetic neuralgia	ヘルペス後神経痛	1 (<0.1%)	0	1 (<0.1%)	0

System Organ Class	器官別大分類	Preferred Term	基本語	Imeglimin 1000 mg bid N = 1103 AE n (%)	Imeglimin 1000 mg bid N = 1103 Serious AE n (%)	Imeglimin All N = 1253 AE n (%)	Imeglimin All N = 1253 Serious AE n (%)
		Somnolence	傾眠	1 (<0.1%)	0	1 (<0.1%)	0
		Spondylitic myelopathy	脊椎炎性脊髄症	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)
		Thoracic outlet syndrome	胸郭出口症候群	0	0	1 (<0.1%)	0
Eye disorders	眼障害	(Total)	（計）	62 (5.6%)	1 (<0.1%)	67 (5.3%)	1 (<0.1%)
		Diabetic retinopathy	糖尿病網膜症	15 (1.4%)	0	15 (1.2%)	0
		Cataract	白内障	6 (0.5%)	0	7 (0.6%)	0
		Dry eye	眼乾燥	6 (0.5%)	0	6 (0.5%)	0
		Glaucoma	緑内障	6 (0.5%)	0	6 (0.5%)	0
		Blepharitis	眼瞼炎	5 (0.5%)	0	5 (0.4%)	0
		Conjunctivitis allergic	アレルギー性結膜炎	5 (0.5%)	0	5 (0.4%)	0
		Asthenopia	眼精疲労	4 (0.4%)	0	4 (0.3%)	0
		Chalazion	霰粒腫	0	0	2 (0.2%)	0
		Diabetic retinal oedema	糖尿病性網膜浮腫	2 (0.2%)	0	2 (0.2%)	0
		Macular oedema	黄斑浮腫	2 (0.2%)	0	2 (0.2%)	0
		Ocular hyperaemia	眼充血	2 (0.2%)	0	2 (0.2%)	0
		Ocular hypertension	高眼圧症	2 (0.2%)	0	2 (0.2%)	0
		Pingueculitis	瞼裂斑炎	2 (0.2%)	0	2 (0.2%)	0
		Posterior capsule opacification	後嚢部混濁	2 (0.2%)	0	2 (0.2%)	0
		Retinal haemorrhage	網膜出血	2 (0.2%)	0	2 (0.2%)	0

System Organ Class	器官別大分類	Preferred Term	基本語	Imeglimin 1000 mg bid N = 1103 AE n (%)	Imeglimin 1000 mg bid N = 1103 Serious AE n (%)	Imeglimin All N = 1253 AE n (%)	Imeglimin All N = 1253 Serious AE n (%)
		Vitreous haemorrhage	硝子体出血	2 (0.2%)	0	2 (0.2%)	0
		Accommodation disorder	調節障害	1 (<0.1%)	0	1 (<0.1%)	0
		Angle closure glaucoma	閉塞隅角緑内障	1 (<0.1%)	0	1 (<0.1%)	0
		Arteriosclerotic retinopathy	動脈硬化性網膜症	1 (<0.1%)	0	1 (<0.1%)	0
		Conjunctival haemorrhage	結膜出血	1 (<0.1%)	0	1 (<0.1%)	0
		Conjunctival hyperaemia	結膜充血	1 (<0.1%)	0	1 (<0.1%)	0
		Eye inflammation	眼の炎症	0	0	1 (<0.1%)	0
		Eye pain	眼痛	1 (<0.1%)	0	1 (<0.1%)	0
		Eye swelling	眼部腫脹	0	0	1 (<0.1%)	0
		Macular fibrosis	黄斑線維症	1 (<0.1%)	0	1 (<0.1%)	0
		Retinal detachment	網膜剥離	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)
		Retinal vein occlusion	網膜静脈閉塞	1 (<0.1%)	0	1 (<0.1%)	0
		Scintillating scotoma	閃輝暗点	1 (<0.1%)	0	1 (<0.1%)	0
		Trichiasis	睫毛乱生	1 (<0.1%)	0	1 (<0.1%)	0
Ear and labyrinth disorders	耳および迷路障害	(Total)	（計）	16 (1.5%)	0	19 (1.5%)	0
		Vertigo	回転性めまい	6 (0.5%)	0	8 (0.6%)	0
		Tinnitus	耳鳴	3 (0.3%)	0	3 (0.2%)	0
		Vertigo positional	頭位性回転性めまい	3 (0.3%)	0	3 (0.2%)	0

System Organ Class	器官別大分類	Preferred Term	基本語	Imeglimin 1000 mg bid N = 1103 AE n (%)	Imeglimin 1000 mg bid N = 1103 Serious AE n (%)	Imeglimin All N = 1253 AE n (%)	Imeglimin All N = 1253 Serious AE n (%)
		Deafness transitory	一過性難聴	1 (<0.1%)	0	1 (<0.1%)	0
		Ear congestion	耳閉	0	0	1 (<0.1%)	0
		External ear inflammation	外耳の炎症	1 (<0.1%)	0	1 (<0.1%)	0
		Meniere's disease	メニエール病	1 (<0.1%)	0	1 (<0.1%)	0
		Middle ear inflammation	中耳の炎症	1 (<0.1%)	0	1 (<0.1%)	0
		Sudden hearing loss	突発性難聴	1 (<0.1%)	0	1 (<0.1%)	0
Cardiac disorders	心臓障害	(Total)	（計）	23 (2.1%)	10 (0.9%)	26 (2.1%)	10 (0.8%)
		Atrial fibrillation	心房細動	5 (0.5%)	1 (<0.1%)	6 (0.5%)	1 (<0.1%)
		Palpitations	動悸	3 (0.3%)	0	4 (0.3%)	0
		Coronary artery stenosis	冠動脈狭窄	3 (0.3%)	3 (0.3%)	3 (0.2%)	3 (0.2%)
		Ventricular extrasystoles	心室性期外収縮	2 (0.2%)	0	3 (0.2%)	0
		Angina unstable	不安定狭心症	2 (0.2%)	2 (0.2%)	2 (0.2%)	2 (0.2%)
		Extrasystoles	期外収縮	2 (0.2%)	0	2 (0.2%)	0
		Sinus bradycardia	洞性徐脈	2 (0.2%)	0	2 (0.2%)	0
		Acute myocardial infarction	急性心筋梗塞	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)
		Aortic valve incompetence	大動脈弁閉鎖不全症	1 (<0.1%)	0	1 (<0.1%)	0
		Bradycardia	徐脈	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)
		Cardiac aneurysm	心臓瘤	1 (<0.1%)	0	1 (<0.1%)	0

System Organ Class	器官別大分類	Preferred Term	基本語	Imeglimin 1000 mg bid N = 1103 AE n (%)	Imeglimin 1000 mg bid N = 1103 Serious AE n (%)	Imeglimin All N = 1253 AE n (%)	Imeglimin All N = 1253 Serious AE n (%)
		Cardiac failure	心不全	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)
		Cardiac failure congestive	うっ血性心不全	1 (<0.1%)	0	1 (<0.1%)	0
		Myocardial infarction	心筋梗塞	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)
		Myocardial ischaemia	心筋虚血	1 (<0.1%)	0	1 (<0.1%)	0
		Sinus tachycardia	洞性頻脈	1 (<0.1%)	0	1 (<0.1%)	0
		Supraventricular extrasystoles	上室性期外収縮	1 (<0.1%)	0	1 (<0.1%)	0
Vascular disorders	血管障害	(Total)	（計）	33 (3.0%)	1 (<0.1%)	36 (2.9%)	1 (<0.1%)
		Hypertension	高血圧	28 (2.5%)	0	31 (2.5%)	0
		Orthostatic hypotension	起立性低血圧	2 (0.2%)	0	2 (0.2%)	0
		Arteriosclerosis	動脈硬化症	1 (<0.1%)	0	1 (<0.1%)	0
		Hypotension	低血圧	1 (<0.1%)	0	1 (<0.1%)	0
		Peripheral arterial occlusive disease	末梢動脈閉塞性疾患	1 (<0.1%)	0	1 (<0.1%)	0
		Venous thrombosis limb	四肢静脈血栓症	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)
Respiratory, thoracic and mediastinal disorders	呼吸器、胸郭および縦隔障害	(Total)	（計）	55 (5.0%)	1 (<0.1%)	60 (4.8%)	1 (<0.1%)
		Upper respiratory tract inflammation	上気道の炎症	16 (1.5%)	0	17 (1.4%)	0
		Cough	咳嗽	11 (1.0%)	0	11 (0.9%)	0
		Rhinitis allergic	アレルギー性鼻炎	6 (0.5%)	0	8 (0.6%)	0

System Organ Class	器官別大分類	Preferred Term	基本語	Imeglimin 1000 mg bid N = 1103 AE n (%)	Imeglimin 1000 mg bid N = 1103 Serious AE n (%)	Imeglimin All N = 1253 AE n (%)	Imeglimin All N = 1253 Serious AE n (%)
		Oropharyngeal pain	口腔咽頭痛	5 (0.5%)	0	7 (0.6%)	0
		Asthma	喘息	6 (0.5%)	0	6 (0.5%)	0
		Bronchitis chronic	慢性気管支炎	3 (0.3%)	0	3 (0.2%)	0
		Epistaxis	鼻出血	3 (0.3%)	0	3 (0.2%)	0
		Sputum increased	喀痰増加	2 (0.2%)	0	2 (0.2%)	0
		Allergic cough	アレルギー性咳嗽	1 (<0.1%)	0	1 (<0.1%)	0
		Hiccups	しゃっくり	1 (<0.1%)	0	1 (<0.1%)	0
		Nasal congestion	鼻閉	1 (<0.1%)	0	1 (<0.1%)	0
		Pleural thickening	胸膜肥厚	1 (<0.1%)	0	1 (<0.1%)	0
		Productive cough	湿性咳嗽	1 (<0.1%)	0	1 (<0.1%)	0
		Pulmonary embolism	肺塞栓症	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)
		Rhinorrhoea	鼻漏	1 (<0.1%)	0	1 (<0.1%)	0
Gastrointestinal disorders	胃腸障害	(Total)	（計）	214 (19.4%)	6 (0.5%)	249 (19.9%)	6 (0.5%)
		Diarrhoea	下痢	40 (3.6%)	0	49 (3.9%)	0
		Nausea	悪心	38 (3.4%)	0	44 (3.5%)	0
		Constipation	便秘	35 (3.2%)	0	37 (3.0%)	0
		Abdominal discomfort	腹部不快感	16 (1.5%)	0	24 (1.9%)	0
		Gastrooesophageal reflux disease	胃食道逆流性疾患	22 (2.0%)	0	24 (1.9%)	0
		Vomiting	嘔吐	15 (1.4%)	0	19 (1.5%)	0

System Organ Class	器官別大分類	Preferred Term	基本語	Imeglimin 1000 mg bid N = 1103 AE n (%)	Imeglimin 1000 mg bid N = 1103 Serious AE n (%)	Imeglimin All N = 1253 AE n (%)	Imeglimin All N = 1253 Serious AE n (%)
		Abdominal pain upper	上腹部痛	15 (1.4%)	0	17 (1.4%)	0
		Dental caries	齲歯	16 (1.5%)	0	17 (1.4%)	0
		Chronic gastritis	慢性胃炎	11 (1.0%)	0	11 (0.9%)	0
		Dyspepsia	消化不良	8 (0.7%)	0	10 (0.8%)	0
		Gastritis	胃炎	8 (0.7%)	0	9 (0.7%)	0
		Large intestine polyp	大腸ポリープ	8 (0.7%)	3 (0.3%)	8 (0.6%)	3 (0.2%)
		Abdominal distension	腹部膨満	5 (0.5%)	0	6 (0.5%)	0
		Abdominal pain	腹痛	6 (0.5%)	0	6 (0.5%)	0
		Faeces soft	軟便	6 (0.5%)	0	6 (0.5%)	0
		Periodontal disease	歯周病	4 (0.4%)	0	5 (0.4%)	0
		Toothache	歯痛	4 (0.4%)	0	4 (0.3%)	0
		Aphthous ulcer	アフタ性潰瘍	3 (0.3%)	0	3 (0.2%)	0
		Stomatitis	口内炎	2 (0.2%)	0	3 (0.2%)	0
		Colitis ulcerative	潰瘍性大腸炎	2 (0.2%)	0	2 (0.2%)	0
		Enteritis	小腸炎	1 (<0.1%)	0	2 (0.2%)	0
		Epigastric discomfort	心窩部不快感	2 (0.2%)	0	2 (0.2%)	0
		Food poisoning	食中毒	2 (0.2%)	0	2 (0.2%)	0
		Abdominal pain lower	下腹部痛	1 (<0.1%)	0	1 (<0.1%)	0
		Abnormal faeces	異常便	1 (<0.1%)	0	1 (<0.1%)	0
		Change of bowel habit	便習慣変化	1 (<0.1%)	0	1 (<0.1%)	0
		Colitis	大腸炎	1 (<0.1%)	0	1 (<0.1%)	0

System Organ Class	器官別大分類	Preferred Term	基本語	Imeglimin 1000 mg bid N = 1103 AE n (%)	Imeglimin 1000 mg bid N = 1103 Serious AE n (%)	Imeglimin All N = 1253 AE n (%)	Imeglimin All N = 1253 Serious AE n (%)
		Diverticulum intestinal	腸憩室	1 (<0.1%)	0	1 (<0.1%)	0
		Duodenal polyp	十二指腸ポリープ	0	0	1 (<0.1%)	0
		Duodenitis	十二指腸炎	0	0	1 (<0.1%)	0
		Enterocolitis	腸炎	1 (<0.1%)	0	1 (<0.1%)	0
		Enterovesical fistula	腸膀胱瘻	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)
		Flatulence	鼓腸	1 (<0.1%)	0	1 (<0.1%)	0
		Gastric polyps	胃ポリープ	1 (<0.1%)	0	1 (<0.1%)	0
		Gastritis erosive	びらん性胃炎	1 (<0.1%)	0	1 (<0.1%)	0
		Gastrointestinal disorder	胃腸障害	1 (<0.1%)	0	1 (<0.1%)	0
		Glossitis	舌炎	1 (<0.1%)	0	1 (<0.1%)	0
		Haematochezia	血便排泄	1 (<0.1%)	0	1 (<0.1%)	0
		Ileus	イレウス	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)
		Inguinal hernia	鼠径ヘルニア	1 (<0.1%)	0	1 (<0.1%)	0
		Irritable bowel syndrome	過敏性腸症候群	1 (<0.1%)	0	1 (<0.1%)	0
		Loose tooth	弛緩歯	1 (<0.1%)	0	1 (<0.1%)	0
		Lower gastrointestinal haemorrhage	下部消化管出血	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)
		Mouth ulceration	口腔内潰瘍形成	1 (<0.1%)	0	1 (<0.1%)	0
		Pancreatic steatosis	膵脂肪変性	1 (<0.1%)	0	1 (<0.1%)	0
		Tooth loss	歯の脱落	1 (<0.1%)	0	1 (<0.1%)	0

System Organ Class	器官別大分類	Preferred Term	基本語	Imeglimin 1000 mg bid N = 1103 AE n (%)	Imeglimin 1000 mg bid N = 1103 Serious AE n (%)	Imeglimin All N = 1253 AE n (%)	Imeglimin All N = 1253 Serious AE n (%)
Hepatobiliary disorders	肝胆道系障害	(Total)	（計）	20 (1.8%)	2 (0.2%)	22 (1.8%)	2 (0.2%)
		Hepatic steatosis	脂肪肝	7 (0.6%)	0	8 (0.6%)	0
		Alcoholic liver disease	アルコール性肝疾患	3 (0.3%)	0	3 (0.2%)	0
		Cholelithiasis	胆石症	3 (0.3%)	0	3 (0.2%)	0
		Drug-induced liver injury	薬物性肝障害	3 (0.3%)	1 (<0.1%)	3 (0.2%)	1 (<0.1%)
		Gallbladder polyp	胆嚢ポリープ	3 (0.3%)	0	3 (0.2%)	0
		Hepatic function abnormal	肝機能異常	2 (0.2%)	1 (<0.1%)	2 (0.2%)	1 (<0.1%)
		Cholecystitis	胆嚢炎	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)
		Hepatomegaly	肝腫大	0	0	1 (<0.1%)	0
		Hyperplastic cholecystopathy	過形成性胆嚢症	1 (<0.1%)	0	1 (<0.1%)	0
		Non-alcoholic steatohepatitis	非アルコール性脂肪性肝炎	1 (<0.1%)	0	1 (<0.1%)	0
Skin and subcutaneous tissue disorders	皮膚および皮下組織障害	(Total)	（計）	69 (6.3%)	0	77 (6.1%)	0
		Eczema	湿疹	25 (2.3%)	0	30 (2.4%)	0
		Acne	ざ瘡	5 (0.5%)	0	5 (0.4%)	0
		Dermatitis	皮膚炎	5 (0.5%)	0	5 (0.4%)	0
		Hyperkeratosis	過角化	4 (0.4%)	0	4 (0.3%)	0
		Dermal cyst	皮膚嚢腫	3 (0.3%)	0	3 (0.2%)	0

System Organ Class	器官別大分類	Preferred Term	基本語	Imeglimin 1000 mg bid N = 1103 AE n (%)	Imeglimin 1000 mg bid N = 1103 Serious AE n (%)	Imeglimin All N = 1253 AE n (%)	Imeglimin All N = 1253 Serious AE n (%)
		Drug eruption	薬疹	3 (0.3%)	0	3 (0.2%)	0
		Dry skin	皮膚乾燥	3 (0.3%)	0	3 (0.2%)	0
		Miliaria	汗疹	2 (0.2%)	0	3 (0.2%)	0
		Urticaria	蕁麻疹	3 (0.3%)	0	3 (0.2%)	0
		Dyshidrotic eczema	異汗性湿疹	2 (0.2%)	0	2 (0.2%)	0
		Eczema asteatotic	皮脂欠乏性湿疹	2 (0.2%)	0	2 (0.2%)	0
		Pruritus	そう痒症	2 (0.2%)	0	2 (0.2%)	0
		Rash	発疹	2 (0.2%)	0	2 (0.2%)	0
		Asteatosis	皮脂欠乏症	1 (<0.1%)	0	1 (<0.1%)	0
		Cold sweat	冷汗	1 (<0.1%)	0	1 (<0.1%)	0
		Dermatitis allergic	アレルギー性皮膚炎	1 (<0.1%)	0	1 (<0.1%)	0
		Dermatitis contact	接触皮膚炎	1 (<0.1%)	0	1 (<0.1%)	0
		Erythema	紅斑	1 (<0.1%)	0	1 (<0.1%)	0
		Haemorrhage subcutaneous	皮下出血	1 (<0.1%)	0	1 (<0.1%)	0
		Hand dermatitis	手皮膚炎	1 (<0.1%)	0	1 (<0.1%)	0
		Ingrowing nail	嵌入爪	0	0	1 (<0.1%)	0
		Leukoderma	白斑	1 (<0.1%)	0	1 (<0.1%)	0
		Nail disorder	爪の障害	1 (<0.1%)	0	1 (<0.1%)	0
		Seborrhoeic dermatitis	脂漏性皮膚炎	1 (<0.1%)	0	1 (<0.1%)	0
		Skin mass	皮膚腫瘤	1 (<0.1%)	0	1 (<0.1%)	0

System Organ Class	器官別大分類	Preferred Term	基本語	Imeglimin 1000 mg bid N = 1103 AE n (%)	Imeglimin 1000 mg bid N = 1103 Serious AE n (%)	Imeglimin All N = 1253 AE n (%)	Imeglimin All N = 1253 Serious AE n (%)
		Xanthoma	黄色腫	0	0	1 (<0.1%)	0
Musculoskeletal and connective tissue disorders	筋骨格系および結合組織障害	(Total)	（計）	141 (12.8%)	2 (0.2%)	155 (12.4%)	2 (0.2%)
		Back pain	背部痛	34 (3.1%)	0	39 (3.1%)	0
		Arthralgia	関節痛	18 (1.6%)	0	20 (1.6%)	0
		Spinal osteoarthritis	変形性脊椎症	13 (1.2%)	0	13 (1.0%)	0
		Muscle spasms	筋痙縮	12 (1.1%)	0	12 (1.0%)	0
		Pain in extremity	四肢痛	10 (0.9%)	0	11 (0.9%)	0
		Intervertebral disc protrusion	椎間板突出	8 (0.7%)	0	9 (0.7%)	0
		Myalgia	筋肉痛	9 (0.8%)	0	9 (0.7%)	0
		Osteoarthritis	変形性関節症	9 (0.8%)	0	9 (0.7%)	0
		Musculoskeletal stiffness	筋骨格硬直	6 (0.5%)	0	7 (0.6%)	0
		Periarthritis	関節周囲炎	6 (0.5%)	0	6 (0.5%)	0
		Trigger finger	弾発指	6 (0.5%)	0	6 (0.5%)	0
		Lumbar spinal stenosis	腰部脊柱管狭窄症	5 (0.5%)	1 (<0.1%)	5 (0.4%)	1 (<0.1%)
		Musculoskeletal pain	筋骨格痛	3 (0.3%)	0	4 (0.3%)	0
		Neck pain	頚部痛	3 (0.3%)	0	4 (0.3%)	0
		Temporomandibular joint syndrome	顎関節症候群	2 (0.2%)	0	3 (0.2%)	0
		Arthritis	関節炎	1 (<0.1%)	0	2 (0.2%)	0

System Organ Class	器官別大分類	Preferred Term	基本語	Imeglimin 1000 mg bid N = 1103 AE n (%)	Imeglimin 1000 mg bid N = 1103 Serious AE n (%)	Imeglimin All N = 1253 AE n (%)	Imeglimin All N = 1253 Serious AE n (%)
		Synovial cyst	滑液嚢腫	2 (0.2%)	0	2 (0.2%)	0
		Synovitis	滑膜炎	2 (0.2%)	1 (<0.1%)	2 (0.2%)	1 (<0.1%)
		Tenosynovitis	腱鞘炎	2 (0.2%)	0	2 (0.2%)	0
		Chondrocalcinosis pyrophosphate	ピロリン酸カルシウム結晶性軟骨石灰化症	1 (<0.1%)	0	1 (<0.1%)	0
		Flank pain	側腹部痛	1 (<0.1%)	0	1 (<0.1%)	0
		Intervertebral disc degeneration	椎間板変性症	1 (<0.1%)	0	1 (<0.1%)	0
		Joint contracture	関節拘縮	1 (<0.1%)	0	1 (<0.1%)	0
		Mastication disorder	咀嚼障害	0	0	1 (<0.1%)	0
		Muscular weakness	筋力低下	1 (<0.1%)	0	1 (<0.1%)	0
		Musculoskeletal chest pain	筋骨格系胸痛	0	0	1 (<0.1%)	0
		Myofascitis	筋筋膜炎	1 (<0.1%)	0	1 (<0.1%)	0
		Nodal osteoarthritis	結節性変形性関節症	1 (<0.1%)	0	1 (<0.1%)	0
		Plantar fasciitis	足底筋膜炎	1 (<0.1%)	0	1 (<0.1%)	0
		Spondylolisthesis	脊椎すべり症	1 (<0.1%)	0	1 (<0.1%)	0
		Tendon pain	腱痛	1 (<0.1%)	0	1 (<0.1%)	0
		Tendonitis	腱炎	1 (<0.1%)	0	1 (<0.1%)	0
Renal and urinary disorders	腎および尿路障害	(Total)	（計）	24 (2.2%)	0	25 (2.0%)	0

System Organ Class	器官別大分類	Preferred Term	基本語	Imeglimin 1000 mg bid N = 1103 AE n (%)	Imeglimin 1000 mg bid N = 1103 Serious AE n (%)	Imeglimin All N = 1253 AE n (%)	Imeglimin All N = 1253 Serious AE n (%)
		Diabetic nephropathy	糖尿病性腎症	7 (0.6%)	0	8 (0.6%)	0
		Nephrolithiasis	腎結石症	7 (0.6%)	0	7 (0.6%)	0
		Pollakiuria	頻尿	3 (0.3%)	0	3 (0.2%)	0
		Haematuria	血尿	2 (0.2%)	0	2 (0.2%)	0
		Renal cyst	腎嚢胞	2 (0.2%)	0	2 (0.2%)	0
		Calculus urinary	尿路結石	1 (<0.1%)	0	1 (<0.1%)	0
		Hypertonic bladder	緊張性膀胱	1 (<0.1%)	0	1 (<0.1%)	0
		Polyuria	多尿	1 (<0.1%)	0	1 (<0.1%)	0
		Ureterolithiasis	尿管結石症	1 (<0.1%)	0	1 (<0.1%)	0
		Urinary tract disorder	尿路障害	1 (<0.1%)	0	1 (<0.1%)	0
Reproductive system and breast disorders	生殖系および乳房障害	(Total)	（計）	14 (1.3%)	1 (<0.1%)	15 (1.2%)	1 (<0.1%)
		Benign prostatic hyperplasia	良性前立腺肥大症	5 (0.5%)	0	5 (0.4%)	0
		Dysmenorrhoea	月経困難症	3 (0.3%)	0	3 (0.2%)	0
		Metrorrhagia	不正子宮出血	1 (<0.1%)	0	2 (0.2%)	0
		Erectile dysfunction	勃起不全	1 (<0.1%)	0	1 (<0.1%)	0
		Genital haemorrhage	性器出血	1 (<0.1%)	0	1 (<0.1%)	0
		Ovarian cyst	卵巣嚢胞	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)
		Prostatitis	前立腺炎	1 (<0.1%)	0	1 (<0.1%)	0
		Prostatomegaly	前立腺腫大	1 (<0.1%)	0	1 (<0.1%)	0

System Organ Class	器官別大分類	Preferred Term	基本語	Imeglimin 1000 mg bid N = 1103 AE n (%)	Imeglimin 1000 mg bid N = 1103 Serious AE n (%)	Imeglimin All N = 1253 AE n (%)	Imeglimin All N = 1253 Serious AE n (%)
		Uterine polyp	子宮ポリープ	1 (<0.1%)	0	1 (<0.1%)	0
Congenital, familial and genetic disorders	先天性、家族性および遺伝性障害	(Total)	（計）	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)
		Dermoid cyst	皮様嚢腫	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)
General disorders and administration site conditions	一般・全身障害および投与部位の状態	(Total)	（計）	27 (2.4%)	2 (0.2%)	33 (2.6%)	2 (0.2%)
		Fatigue	疲労	7 (0.6%)	0	9 (0.7%)	0
		Pyrexia	発熱	6 (0.5%)	0	6 (0.5%)	0
		Malaise	倦怠感	2 (0.2%)	0	4 (0.3%)	0
		Oedema peripheral	末梢性浮腫	2 (0.2%)	0	3 (0.2%)	0
		Chest discomfort	胸部不快感	2 (0.2%)	0	2 (0.2%)	0
		Chest pain	胸痛	2 (0.2%)	0	2 (0.2%)	0
		Non-cardiac chest pain	非心臓性胸痛	2 (0.2%)	0	2 (0.2%)	0
		Early satiety	早期満腹	1 (<0.1%)	0	1 (<0.1%)	0
		Feeling abnormal	異常感	0	0	1 (<0.1%)	0
		Inflammation	炎症	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)
		Sudden death	突然死	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)
		Thirst	口渇	1 (<0.1%)	0	1 (<0.1%)	0
Investigations	臨床検査	(Total)	（計）	43 (3.9%)	0	54 (4.3%)	0

System Organ Class	器官別大分類	Preferred Term	基本語	Imeglimin 1000 mg bid N = 1103 AE n (%)	Imeglimin 1000 mg bid N = 1103 Serious AE n (%)	Imeglimin All N = 1253 AE n (%)	Imeglimin All N = 1253 Serious AE n (%)
		Lipase increased	リパーゼ増加	8 (0.7%)	0	9 (0.7%)	0
		Blood creatine phosphokinase increased	血中クレアチンホスホキナーゼ増加	6 (0.5%)	0	6 (0.5%)	0
		Weight decreased	体重減少	6 (0.5%)	0	6 (0.5%)	0
		Culture urine positive	尿培養陽性	0	0	5 (0.4%)	0
		Amylase increased	アミラーゼ増加	4 (0.4%)	0	4 (0.3%)	0
		Blood lactic acid increased	血中乳酸増加	3 (0.3%)	0	3 (0.2%)	0
		Gamma-glutamyltransferase increased	γ－グルタミルトランスフェラーゼ増加	2 (0.2%)	0	3 (0.2%)	0
		Hepatic enzyme increased	肝酵素上昇	3 (0.3%)	0	3 (0.2%)	0
		C-reactive protein increased	Ｃ－反応性蛋白増加	2 (0.2%)	0	2 (0.2%)	0
		Occult blood	便潜血	1 (<0.1%)	0	2 (0.2%)	0
		Platelet count decreased	血小板数減少	2 (0.2%)	0	2 (0.2%)	0
		Activated partial thromboplastin time prolonged	活性化部分トロンボプラスチン時間延長	0	0	1 (<0.1%)	0
		Aspartate aminotransferase increased	アスパラギン酸アミノトランスフェラーゼ増加	1 (<0.1%)	0	1 (<0.1%)	0
		Blood alkaline phosphatase increased	血中アルカリホスファターゼ増加	1 (<0.1%)	0	1 (<0.1%)	0

System Organ Class	器官別大分類	Preferred Term	基本語	Imeglimin 1000 mg bid N = 1103 AE n (%)	Imeglimin 1000 mg bid N = 1103 Serious AE n (%)	Imeglimin All N = 1253 AE n (%)	Imeglimin All N = 1253 Serious AE n (%)
		Blood creatinine increased	血中クレアチニン増加	1 (<0.1%)	0	1 (<0.1%)	0
		Blood glucagon increased	血中グルカゴン増加	0	0	1 (<0.1%)	0
		Blood glucose abnormal	血中ブドウ糖異常	1 (<0.1%)	0	1 (<0.1%)	0
		Electrocardiogram T wave inversion	心電図Ｔ波逆転	0	0	1 (<0.1%)	0
		Electrocardiogram repolarisation abnormality	心電図再分極異常	1 (<0.1%)	0	1 (<0.1%)	0
		Eosinophil count increased	好酸球数増加	0	0	1 (<0.1%)	0
		International normalised ratio increased	国際標準比増加	0	0	1 (<0.1%)	0
		Intraocular pressure increased	眼圧上昇	1 (<0.1%)	0	1 (<0.1%)	0
		Liver function test increased	肝機能検査値上昇	1 (<0.1%)	0	1 (<0.1%)	0
		Neutrophil count decreased	好中球数減少	1 (<0.1%)	0	1 (<0.1%)	0
		Occult blood positive	便潜血陽性	1 (<0.1%)	0	1 (<0.1%)	0
		Urine albumin/creatinine ratio increased	尿中アルブミン／クレアチニン比増加	1 (<0.1%)	0	1 (<0.1%)	0
		White blood cell count increased	白血球数増加	1 (<0.1%)	0	1 (<0.1%)	0
Injury, poisoning and procedural complications	傷害、中毒および処置合併症	(Total)	（計）	90 (8.2%)	13 (1.2%)	101 (8.1%)	13 (1.0%)

System Organ Class	器官別大分類	Preferred Term	基本語	Imeglimin 1000 mg bid N = 1103 AE n (%)	Imeglimin 1000 mg bid N = 1103 Serious AE n (%)	Imeglimin All N = 1253 AE n (%)	Imeglimin All N = 1253 Serious AE n (%)
		Contusion	挫傷	15 (1.4%)	1 (<0.1%)	18 (1.4%)	1 (<0.1%)
		Ligament sprain	靱帯捻挫	8 (0.7%)	0	9 (0.7%)	0
		Arthropod sting	節足動物刺傷	3 (0.3%)	0	7 (0.6%)	0
		Thermal burn	熱傷	6 (0.5%)	0	6 (0.5%)	0
		Hand fracture	手骨折	3 (0.3%)	0	5 (0.4%)	0
		Heat illness	熱中症	5 (0.5%)	1 (<0.1%)	5 (0.4%)	1 (<0.1%)
		Radius fracture	橈骨骨折	4 (0.4%)	1 (<0.1%)	5 (0.4%)	1 (<0.1%)
		Rib fracture	肋骨骨折	4 (0.4%)	0	5 (0.4%)	0
		Wound	創傷	4 (0.4%)	0	4 (0.3%)	0
		Arthropod bite	節足動物咬傷	3 (0.3%)	0	3 (0.2%)	0
		Clavicle fracture	鎖骨骨折	3 (0.3%)	3 (0.3%)	3 (0.2%)	3 (0.2%)
		Foot fracture	足骨折	3 (0.3%)	0	3 (0.2%)	0
		Muscle strain	肉離れ	3 (0.3%)	0	3 (0.2%)	0
		Skin abrasion	皮膚擦過傷	3 (0.3%)	0	3 (0.2%)	0
		Avulsion fracture	剥離骨折	2 (0.2%)	0	2 (0.2%)	0
		Ligament injury	靱帯損傷	2 (0.2%)	0	2 (0.2%)	0
		Post procedural haemorrhage	処置後出血	2 (0.2%)	1 (<0.1%)	2 (0.2%)	1 (<0.1%)
		Stress fracture	ストレス骨折	2 (0.2%)	0	2 (0.2%)	0
		Tendon rupture	腱断裂	2 (0.2%)	0	2 (0.2%)	0
		Animal bite	動物咬傷	1 (<0.1%)	0	1 (<0.1%)	0

System Organ Class	器官別大分類	Preferred Term	基本語	Imeglimin 1000 mg bid N = 1103 AE n (%)	Imeglimin 1000 mg bid N = 1103 Serious AE n (%)	Imeglimin All N = 1253 AE n (%)	Imeglimin All N = 1253 Serious AE n (%)
		Bone contusion	骨挫傷	0	0	1 (<0.1%)	0
		Closed globe injury	閉鎖性眼球損傷	1 (<0.1%)	0	1 (<0.1%)	0
		Concussion	脳振盪	1 (<0.1%)	0	1 (<0.1%)	0
		Craniocerebral injury	頭蓋脳損傷	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)
		Epicondylitis	上顆炎	1 (<0.1%)	0	1 (<0.1%)	0
		Fall	転倒	0	0	1 (<0.1%)	0
		Femur fracture	大腿骨骨折	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)
		Fractured coccyx	尾骨骨折	1 (<0.1%)	0	1 (<0.1%)	0
		Fractured ischium	坐骨骨折	1 (<0.1%)	0	1 (<0.1%)	0
		Heat stroke	熱射病	1 (<0.1%)	0	1 (<0.1%)	0
		Laceration	裂傷	1 (<0.1%)	0	1 (<0.1%)	0
		Lower limb fracture	下肢骨折	1 (<0.1%)	0	1 (<0.1%)	0
		Meniscus injury	半月板損傷	1 (<0.1%)	0	1 (<0.1%)	0
		Multiple fractures	多発骨折	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)
		Nasal injury	鼻部損傷	1 (<0.1%)	0	1 (<0.1%)	0
		Pneumothorax traumatic	外傷性気胸	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)
		Post-traumatic neck syndrome	外傷後頚部症候群	1 (<0.1%)	0	1 (<0.1%)	0
		Procedural pain	処置による疼痛	1 (<0.1%)	0	1 (<0.1%)	0
		Pubis fracture	恥骨骨折	1 (<0.1%)	0	1 (<0.1%)	0
		Scratch	引っかき傷	1 (<0.1%)	0	1 (<0.1%)	0

System Organ Class	器官別大分類	Preferred Term	基本語	Imeglimin 1000 mg bid N = 1103 AE n (%)	Imeglimin 1000 mg bid N = 1103 Serious AE n (%)	Imeglimin All N = 1253 AE n (%)	Imeglimin All N = 1253 Serious AE n (%)
		Spinal compression fracture	脊椎圧迫骨折	1 (<0.1%)	0	1 (<0.1%)	0
		Spinal fracture	脊椎骨折	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)
		Subarachnoid haemorrhage	くも膜下出血	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)
		Subdural haematoma	硬膜下血腫	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)
		Tooth fracture	歯牙破折	1 (<0.1%)	0	1 (<0.1%)	0
		Traumatic intracranial haemorrhage	外傷性頭蓋内出血	1 (<0.1%)	0	1 (<0.1%)	0
Surgical and medical procedures	外科および内科処置	(Total)	（計）	13 (1.2%)	0	13 (1.0%)	0
		Cataract operation	白内障手術	8 (0.7%)	0	8 (0.6%)	0
		Large intestinal polypectomy	大腸ポリープ切除	2 (0.2%)	0	2 (0.2%)	0
		Blepharoplasty	眼瞼形成	1 (<0.1%)	0	1 (<0.1%)	0
		Endodontic procedure	歯内療法	1 (<0.1%)	0	1 (<0.1%)	0
		Ptosis repair	眼瞼下垂修復	1 (<0.1%)	0	1 (<0.1%)	0
Product issues	製品の問題	(Total)	（計）	1 (<0.1%)	0	1 (<0.1%)	0
		Device dislocation	医療機器位置異常	1 (<0.1%)	0	1 (<0.1%)	0

- Abbreviations: bid, Twice a day; AE, Adverse event; TEAE, Treatment Emergent AE
- All adverse events were coded using MedDRA dictionary version 20.1.
- Percentages are based on Population N.

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Table S-161 Summary of Treatment Emergent Adverse Events Related to Treatment by System Organ Class and Preferred Term in All Patients Treated Imeglimin (PXL008-014, PXL008-018, PXL008-019, PXL008-020; Safety Population, Long-term Safety Population)

				Imeglimin 1000 mg bid N = 1103		Imeglimin All N = 1253	
System Organ Class	器官別大分類	Preferred Term	基本語	AE n (%)	Serious AE n (%)	AE n (%)	Serious AE n (%)
Any TEAE related to treatment	全事象	(Total)	（計）	168 (15.2%)	0	190 (15.2%)	0
Infections and infestations	感染症および寄生虫症	(Total)	（計）	4 (0.4%)	0	4 (0.3%)	0
		Cystitis	膀胱炎	2 (0.2%)	0	2 (0.2%)	0
		Herpes zoster	帯状疱疹	1 (<0.1%)	0	1 (<0.1%)	0
		Impetigo	膿痂疹	1 (<0.1%)	0	1 (<0.1%)	0
		Otitis media acute	急性中耳炎	1 (<0.1%)	0	1 (<0.1%)	0
Blood and lymphatic system disorders	血液およびリンパ系障害	(Total)	（計）	1 (<0.1%)	0	1 (<0.1%)	0
		Anaemia	貧血	1 (<0.1%)	0	1 (<0.1%)	0
Metabolism and nutrition disorders	代謝および栄養障害	(Total)	（計）	84 (7.6%)	0	90 (7.2%)	0
		Hypoglycaemia	低血糖	74 (6.7%)	0	79 (6.3%)	0
		Decreased appetite	食欲減退	9 (0.8%)	0	9 (0.7%)	0
		Hyperglycaemia	高血糖	1 (<0.1%)	0	2 (0.2%)	0
Psychiatric disorders	精神障害	(Total)	（計）	1 (<0.1%)	0	1 (<0.1%)	0

System Organ Class	器官別大分類	Preferred Term	基本語	Imeglimin 1000 mg bid N = 1103 AE n (%)	Imeglimin 1000 mg bid N = 1103 Serious AE n (%)	Imeglimin All N = 1253 AE n (%)	Imeglimin All N = 1253 Serious AE n (%)
		Insomnia	不眠症	1 (<0.1%)	0	1 (<0.1%)	0
Nervous system disorders	神経系障害	(Total)	（計）	2 (0.2%)	0	2 (0.2%)	0
		Diabetic neuropathy	糖尿病性ニューロパチー	1 (<0.1%)	0	1 (<0.1%)	0
		Dysaesthesia	異常感覚	1 (<0.1%)	0	1 (<0.1%)	0
Eye disorders	眼障害	(Total)	（計）	7 (0.6%)	0	7 (0.6%)	0
		Diabetic retinopathy	糖尿病網膜症	4 (0.4%)	0	4 (0.3%)	0
		Diabetic retinal oedema	糖尿病性網膜浮腫	1 (<0.1%)	0	1 (<0.1%)	0
		Glaucoma	緑内障	1 (<0.1%)	0	1 (<0.1%)	0
		Macular oedema	黄斑浮腫	1 (<0.1%)	0	1 (<0.1%)	0
Cardiac disorders	心臓障害	(Total)	（計）	2 (0.2%)	0	2 (0.2%)	0
		Atrial fibrillation	心房細動	1 (<0.1%)	0	1 (<0.1%)	0
		Palpitations	動悸	1 (<0.1%)	0	1 (<0.1%)	0
		Supraventricular extrasystoles	上室性期外収縮	1 (<0.1%)	0	1 (<0.1%)	0
Gastrointestinal disorders	胃腸障害	(Total)	（計）	71 (6.4%)	0	84 (6.7%)	0
		Nausea	悪心	23 (2.1%)	0	27 (2.2%)	0
		Diarrhoea	下痢	21 (1.9%)	0	24 (1.9%)	0

System Organ Class	器官別大分類	Preferred Term	基本語	Imeglimin 1000 mg bid N = 1103 AE n (%)	Imeglimin 1000 mg bid N = 1103 Serious AE n (%)	Imeglimin All N = 1253 AE n (%)	Imeglimin All N = 1253 Serious AE n (%)
		Constipation	便秘	14 (1.3%)	0	14 (1.1%)	0
		Abdominal discomfort	腹部不快感	8 (0.7%)	0	12 (1.0%)	0
		Vomiting	嘔吐	10 (0.9%)	0	12 (1.0%)	0
		Dyspepsia	消化不良	3 (0.3%)	0	4 (0.3%)	0
		Abdominal pain upper	上腹部痛	3 (0.3%)	0	3 (0.2%)	0
		Faeces soft	軟便	3 (0.3%)	0	3 (0.2%)	0
		Abdominal distension	腹部膨満	2 (0.2%)	0	2 (0.2%)	0
		Gastrooesophageal reflux disease	胃食道逆流性疾患	2 (0.2%)	0	2 (0.2%)	0
		Chronic gastritis	慢性胃炎	1 (<0.1%)	0	1 (<0.1%)	0
		Colitis	大腸炎	1 (<0.1%)	0	1 (<0.1%)	0
		Colitis ulcerative	潰瘍性大腸炎	1 (<0.1%)	0	1 (<0.1%)	0
		Epigastric discomfort	心窩部不快感	1 (<0.1%)	0	1 (<0.1%)	0
		Gastritis	胃炎	1 (<0.1%)	0	1 (<0.1%)	0
		Stomatitis	口内炎	0	0	1 (<0.1%)	0
Hepatobiliary disorders	肝胆道系障害	(Total)	（計）	1 (<0.1%)	0	1 (<0.1%)	0
		Hyperplastic cholecystopathy	過形成性胆嚢症	1 (<0.1%)	0	1 (<0.1%)	0
Skin and subcutaneous tissue disorders	皮膚および皮下組織障害	(Total)	（計）	2 (0.2%)	0	2 (0.2%)	0
		Drug eruption	薬疹	1 (<0.1%)	0	1 (<0.1%)	0

System Organ Class	器官別大分類	Preferred Term	基本語	Imeglimin 1000 mg bid N = 1103 AE n (%)	Imeglimin 1000 mg bid N = 1103 Serious AE n (%)	Imeglimin All N = 1253 AE n (%)	Imeglimin All N = 1253 Serious AE n (%)
		Urticaria	蕁麻疹	1 (<0.1%)	0	1 (<0.1%)	0
Musculoskeletal and connective tissue disorders	筋骨格系および結合組織障害	(Total)	（計）	1 (<0.1%)	0	2 (0.2%)	0
		Intervertebral disc protrusion	椎間板突出	1 (<0.1%)	0	1 (<0.1%)	0
		Temporomandibular joint syndrome	顎関節症候群	0	0	1 (<0.1%)	0
Reproductive system and breast disorders	生殖系および乳房障害	(Total)	（計）	1 (<0.1%)	0	1 (<0.1%)	0
		Erectile dysfunction	勃起不全	1 (<0.1%)	0	1 (<0.1%)	0
General disorders and administration site conditions	一般・全身障害および投与部位の状態	(Total)	（計）	2 (0.2%)	0	4 (0.3%)	0
		Malaise	倦怠感	1 (<0.1%)	0	2 (0.2%)	0
		Early satiety	早期満腹	1 (<0.1%)	0	1 (<0.1%)	0
		Feeling abnormal	異常感	0	0	1 (<0.1%)	0
Investigations	臨床検査	(Total)	（計）	9 (0.8%)	0	11 (0.9%)	0
		Blood lactic acid increased	血中乳酸増加	2 (0.2%)	0	2 (0.2%)	0
		Lipase increased	リパーゼ増加	2 (0.2%)	0	2 (0.2%)	0
		Weight decreased	体重減少	2 (0.2%)	0	2 (0.2%)	0

System Organ Class	器官別大分類	Preferred Term	基本語	Imeglimin 1000 mg bid N = 1103 AE n (%)	Imeglimin 1000 mg bid N = 1103 Serious AE n (%)	Imeglimin All N = 1253 AE n (%)	Imeglimin All N = 1253 Serious AE n (%)
		Activated partial thromboplastin time prolonged	活性化部分トロンボプラスチン時間延長	0	0	1 (<0.1%)	0
		Amylase increased	アミラーゼ増加	1 (<0.1%)	0	1 (<0.1%)	0
		Blood glucagon increased	血中グルカゴン増加	0	0	1 (<0.1%)	0
		Culture urine positive	尿培養陽性	0	0	1 (<0.1%)	0
		Electrocardiogram repolarisation abnormality	心電図再分極異常	1 (<0.1%)	0	1 (<0.1%)	0
		International normalised ratio increased	国際標準比増加	0	0	1 (<0.1%)	0
		Liver function test increased	肝機能検査値上昇	1 (<0.1%)	0	1 (<0.1%)	0
		Platelet count decreased	血小板数減少	1 (<0.1%)	0	1 (<0.1%)	0
		Urine albumin/creatinine ratio increased	尿中アルブミン／クレアチニン比増加	1 (<0.1%)	0	1 (<0.1%)	0

- Abbreviations: bid, Twice a day; AE, Adverse event; TEAE, Treatment Emergent AE
- All adverse events were coded using MedDRA dictionary version 20.1.
- Percentages are based on Population N.

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Table S-162 Subgroup Analysis of Treatment Emergent Adverse Events by Age, System Organ Class and Preferred Term in 24-Week Double-blind Period with Monotherapy (PXL008-014, PXL008-018; Safety Population)

System Organ Class Preferred Term Age	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
Number of patients					
< 65 years	106	54	97	47	198
>= 65 years	76	21	83	28	132
< 75 years	169	75	171	75	321
>= 75 years	13	0	9	0	9
Any TEAE					
< 65 years	63 (59.4%)	40 (74.1%)	49 (50.5%)	37 (78.7%)	126 (63.6%)
>= 65 years	36 (47.4%)	11 (52.4%)	44 (53.0%)	18 (64.3%)	73 (55.3%)
< 75 years	93 (55.0%)	51 (68.0%)	86 (50.3%)	55 (73.3%)	192 (59.8%)
>= 75 years	6 (46.2%)	.	7 (77.8%)	.	7 (77.8%)
Infections and infestations (感染症および寄生虫症)					
< 65 years	21 (19.8%)	21 (38.9%)	27 (27.8%)	16 (34.0%)	64 (32.3%)
>= 65 years	11 (14.5%)	6 (28.6%)	23 (27.7%)	10 (35.7%)	39 (29.5%)
< 75 years	30 (17.8%)	27 (36.0%)	48 (28.1%)	26 (34.7%)	101 (31.5%)
>= 75 years	2 (15.4%)	.	2 (22.2%)	.	2 (22.2%)
Nasopharyngitis (上咽頭炎)					
< 65 years	15 (14.2%)	15 (27.8%)	20 (20.6%)	11 (23.4%)	46 (23.2%)
>= 65 years	5 (6.6%)	5 (23.8%)	13 (15.7%)	7 (25.0%)	25 (18.9%)
< 75 years	20 (11.8%)	20 (26.7%)	32 (18.7%)	18 (24.0%)	70 (21.8%)
>= 75 years	0	.	1 (11.1%)	.	1 (11.1%)
Bronchitis (気管支炎)					
< 65 years	0	3 (5.6%)	1 (1.0%)	1 (2.1%)	5 (2.5%)
>= 65 years	1 (1.3%)	0	1 (1.2%)	0	1 (0.8%)
< 75 years	1 (0.6%)	3 (4.0%)	2 (1.2%)	1 (1.3%)	6 (1.9%)
>= 75 years	0	.	0	.	0
Gastroenteritis (胃腸炎)					
< 65 years	2 (1.9%)	1 (1.9%)	1 (1.0%)	0	2 (1.0%)
>= 65 years	0	1 (4.8%)	1 (1.2%)	0	2 (1.5%)
< 75 years	2 (1.2%)	2 (2.7%)	2 (1.2%)	0	4 (1.2%)
>= 75 years	0	.	0	.	0
Pharyngitis (咽頭炎)					
< 65 years	1 (0.9%)	1 (1.9%)	0	0	1 (0.5%)
>= 65 years	1 (1.3%)	0	3 (3.6%)	0	3 (2.3%)
< 75 years	2 (1.2%)	1 (1.3%)	3 (1.8%)	0	4 (1.2%)
>= 75 years	0	.	0	.	0
Periodontitis (歯周炎)					
< 65 years	1 (0.9%)	0	0	1 (2.1%)	1 (0.5%)
>= 65 years	1 (1.3%)	1 (4.8%)	1 (1.2%)	0	2 (1.5%)
< 75 years	1 (0.6%)	1 (1.3%)	1 (0.6%)	1 (1.3%)	3 (0.9%)
>= 75 years	1 (7.7%)	.	0	.	0
Influenza (インフルエンザ)					
< 65 years	0	0	1 (1.0%)	1 (2.1%)	2 (1.0%)

System Organ Class Preferred Term Age	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
>= 65 years	0	0	2 (2.4%)	0	2 (1.5%)
< 75 years	0	0	2 (1.2%)	1 (1.3%)	3 (0.9%)
>= 75 years	0	.	1 (11.1%)	.	1 (11.1%)
Upper respiratory tract infection (上気道感染)					
< 65 years	1 (0.9%)	0	0	1 (2.1%)	1 (0.5%)
>= 65 years	1 (1.3%)	0	1 (1.2%)	0	1 (0.8%)
< 75 years	1 (0.6%)	0	1 (0.6%)	1 (1.3%)	2 (0.6%)
>= 75 years	1 (7.7%)	.	0	.	0
Conjunctivitis (結膜炎)					
< 65 years	0	0	2 (2.1%)	0	2 (1.0%)
>= 65 years	0	0	1 (1.2%)	0	1 (0.8%)
< 75 years	0	0	3 (1.8%)	0	3 (0.9%)
>= 75 years	0	.	0	.	0
Cystitis (膀胱炎)					
< 65 years	1 (0.9%)	1 (1.9%)	0	0	1 (0.5%)
>= 65 years	0	1 (4.8%)	0	0	1 (0.8%)
< 75 years	1 (0.6%)	2 (2.7%)	0	0	2 (0.6%)
>= 75 years	0	.	0	.	0
Otitis externa (外耳炎)					
< 65 years	1 (0.9%)	0	1 (1.0%)	0	1 (0.5%)
>= 65 years	0	0	0	1 (3.6%)	1 (0.8%)
< 75 years	1 (0.6%)	0	1 (0.6%)	1 (1.3%)	2 (0.6%)
>= 75 years	0	.	0	.	0
Gastroenteritis viral (ウイルス性胃腸炎)					
< 65 years	1 (0.9%)	0	0	0	0
>= 65 years	0	0	0	1 (3.6%)	1 (0.8%)
< 75 years	1 (0.6%)	0	0	1 (1.3%)	1 (0.3%)
>= 75 years	0	.	0	.	0
Herpes zoster (帯状疱疹)					
< 65 years	0	0	0	1 (2.1%)	1 (0.5%)
>= 65 years	1 (1.3%)	0	0	0	0
< 75 years	1 (0.6%)	0	0	1 (1.3%)	1 (0.3%)
>= 75 years	0	.	0	.	0
Infected dermal cyst (感染性皮膚嚢腫)					
< 65 years	1 (0.9%)	0	0	0	0
>= 65 years	0	0	1 (1.2%)	0	1 (0.8%)
< 75 years	1 (0.6%)	0	1 (0.6%)	0	1 (0.3%)
>= 75 years	0	.	0	.	0
Oral herpes (口腔ヘルペス)					
< 65 years	1 (0.9%)	0	0	0	0
>= 65 years	1 (1.3%)	0	0	0	0
< 75 years	2 (1.2%)	0	0	0	0
>= 75 years	0	.	0	.	0

System Organ Class Preferred Term Age	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
Asymptomatic bacteriuria (無症候性細菌尿)					
< 65 years	0	0	1 (1.0%)	0	1 (0.5%)
>= 65 years	0	0	0	0	0
< 75 years	0	0	1 (0.6%)	0	1 (0.3%)
>= 75 years	0	.	0	.	0
Bronchitis bacterial (細菌性気管支炎)					
< 65 years	0	0	1 (1.0%)	0	1 (0.5%)
>= 65 years	0	0	0	0	0
< 75 years	0	0	1 (0.6%)	0	1 (0.3%)
>= 75 years	0	.	0	.	0
Conjunctivitis bacterial (細菌性結膜炎)					
< 65 years	0	0	0	0	0
>= 65 years	0	0	0	1 (3.6%)	1 (0.8%)
< 75 years	0	0	0	1 (1.3%)	1 (0.3%)
>= 75 years	0	.	0	.	0
Gingivitis (歯肉炎)					
< 65 years	1 (0.9%)	0	0	0	0
>= 65 years	0	0	0	0	0
< 75 years	1 (0.6%)	0	0	0	0
>= 75 years	0	.	0	.	0
Helicobacter infection (ヘリコバクター感染)					
< 65 years	0	0	0	0	0
>= 65 years	1 (1.3%)	0	0	0	0
< 75 years	1 (0.6%)	0	0	0	0
>= 75 years	0	.	0	.	0
Hordeolum (麦粒腫)					
< 65 years	0	0	0	0	0
>= 65 years	0	0	1 (1.2%)	0	1 (0.8%)
< 75 years	0	0	1 (0.6%)	0	1 (0.3%)
>= 75 years	0	.	0	.	0
Parotitis (耳下腺炎)					
< 65 years	0	0	0	1 (2.1%)	1 (0.5%)
>= 65 years	0	0	0	0	0
< 75 years	0	0	0	1 (1.3%)	1 (0.3%)
>= 75 years	0	.	0	.	0
Pericoronitis (歯冠周囲炎)					
< 65 years	0	0	0	1 (2.1%)	1 (0.5%)
>= 65 years	0	0	0	0	0
< 75 years	0	0	0	1 (1.3%)	1 (0.3%)
>= 75 years	0	.	0	.	0
Pharyngitis streptococcal (レンサ球菌性咽頭炎)					
< 65 years	0	0	0	0	0
>= 65 years	1 (1.3%)	0	0	0	0

System Organ Class Preferred Term Age	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
< 75 years	1 (0.6%)	0	0	0	0
>= 75 years	0	.	0	.	0
Pulpitis dental (歯髄炎)					
< 65 years	0	1 (1.9%)	0	0	1 (0.5%)
>= 65 years	0	0	0	0	0
< 75 years	0	1 (1.3%)	0	0	1 (0.3%)
>= 75 years	0	.	0	.	0
Tooth abscess (歯膿瘍)					
< 65 years	1 (0.9%)	0	0	0	0
>= 65 years	0	0	0	0	0
< 75 years	1 (0.6%)	0	0	0	0
>= 75 years	0	.	0	.	0
Gastrointestinal disorders (胃腸障害)					
< 65 years	12 (11.3%)	10 (18.5%)	14 (14.4%)	14 (29.8%)	38 (19.2%)
>= 65 years	8 (10.5%)	1 (4.8%)	12 (14.5%)	10 (35.7%)	23 (17.4%)
< 75 years	20 (11.8%)	11 (14.7%)	25 (14.6%)	24 (32.0%)	60 (18.7%)
>= 75 years	0	.	1 (11.1%)	.	1 (11.1%)
Diarrhoea (下痢)					
< 65 years	1 (0.9%)	3 (5.6%)	3 (3.1%)	5 (10.6%)	11 (5.6%)
>= 65 years	0	0	2 (2.4%)	1 (3.6%)	3 (2.3%)
< 75 years	1 (0.6%)	3 (4.0%)	5 (2.9%)	6 (8.0%)	14 (4.4%)
>= 75 years	0	.	0	.	0
Abdominal discomfort (腹部不快感)					
< 65 years	0	1 (1.9%)	1 (1.0%)	4 (8.5%)	6 (3.0%)
>= 65 years	0	0	2 (2.4%)	3 (10.7%)	5 (3.8%)
< 75 years	0	1 (1.3%)	3 (1.8%)	7 (9.3%)	11 (3.4%)
>= 75 years	0	.	0	.	0
Vomiting (嘔吐)					
< 65 years	2 (1.9%)	0	1 (1.0%)	2 (4.3%)	3 (1.5%)
>= 65 years	2 (2.6%)	0	0	2 (7.1%)	2 (1.5%)
< 75 years	4 (2.4%)	0	1 (0.6%)	4 (5.3%)	5 (1.6%)
>= 75 years	0	.	0	.	0
Nausea (悪心)					
< 65 years	1 (0.9%)	1 (1.9%)	0	3 (6.4%)	4 (2.0%)
>= 65 years	0	0	1 (1.2%)	2 (7.1%)	3 (2.3%)
< 75 years	1 (0.6%)	1 (1.3%)	1 (0.6%)	5 (6.7%)	7 (2.2%)
>= 75 years	0	.	0	.	0
Dental caries (齲歯)					
< 65 years	3 (2.8%)	0	2 (2.1%)	1 (2.1%)	3 (1.5%)
>= 65 years	1 (1.3%)	0	0	0	0
< 75 years	4 (2.4%)	0	2 (1.2%)	1 (1.3%)	3 (0.9%)
>= 75 years	0	.	0	.	0
Constipation (便秘)					
< 65 years	1 (0.9%)	1 (1.9%)	1 (1.0%)	0	2 (1.0%)
>= 65 years	1 (1.3%)	0	1 (1.2%)	1 (3.6%)	2 (1.5%)

System Organ Class Preferred Term Age	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
< 75 years	2 (1.2%)	1 (1.3%)	2 (1.2%)	1 (1.3%)	4 (1.2%)
>= 75 years	0	.	0	.	0
Abdominal pain upper (上腹部痛)					
< 65 years	1 (0.9%)	1 (1.9%)	0	0	1 (0.5%)
>= 65 years	0	1 (4.8%)	1 (1.2%)	0	2 (1.5%)
< 75 years	1 (0.6%)	2 (2.7%)	1 (0.6%)	0	3 (0.9%)
>= 75 years	0	.	0	.	0
Gastrooesophageal reflux disease (胃食道逆流性疾患)					
< 65 years	0	1 (1.9%)	1 (1.0%)	1 (2.1%)	3 (1.5%)
>= 65 years	1 (1.3%)	0	0	0	0
< 75 years	1 (0.6%)	1 (1.3%)	1 (0.6%)	1 (1.3%)	3 (0.9%)
>= 75 years	0	.	0	.	0
Dyspepsia (消化不良)					
< 65 years	0	1 (1.9%)	1 (1.0%)	1 (2.1%)	3 (1.5%)
>= 65 years	0	0	0	0	0
< 75 years	0	1 (1.3%)	1 (0.6%)	1 (1.3%)	3 (0.9%)
>= 75 years	0	.	0	.	0
Gastritis (胃炎)					
< 65 years	0	1 (1.9%)	1 (1.0%)	0	2 (1.0%)
>= 65 years	0	0	1 (1.2%)	0	1 (0.8%)
< 75 years	0	1 (1.3%)	2 (1.2%)	0	3 (0.9%)
>= 75 years	0	.	0	.	0
Periodontal disease (歯周病)					
< 65 years	1 (0.9%)	1 (1.9%)	0	0	1 (0.5%)
>= 65 years	0	0	1 (1.2%)	0	1 (0.8%)
< 75 years	1 (0.6%)	1 (1.3%)	1 (0.6%)	0	2 (0.6%)
>= 75 years	0	.	0	.	0
Abdominal distension (腹部膨満)					
< 65 years	0	0	0	0	0
>= 65 years	0	0	1 (1.2%)	1 (3.6%)	2 (1.5%)
< 75 years	0	0	1 (0.6%)	1 (1.3%)	2 (0.6%)
>= 75 years	0	.	0	.	0
Abdominal pain (腹痛)					
< 65 years	0	0	2 (2.1%)	0	2 (1.0%)
>= 65 years	0	0	0	0	0
< 75 years	0	0	2 (1.2%)	0	2 (0.6%)
>= 75 years	0	.	0	.	0
Chronic gastritis (慢性胃炎)					
< 65 years	0	0	1 (1.0%)	0	1 (0.5%)
>= 65 years	0	0	1 (1.2%)	0	1 (0.8%)
< 75 years	0	0	2 (1.2%)	0	2 (0.6%)
>= 75 years	0	.	0	.	0
Duodenal ulcer (十二指腸潰瘍)					
< 65 years	1 (0.9%)	0	0	0	0
>= 65 years	1 (1.3%)	0	0	0	0

System Organ Class Preferred Term Age	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
< 75 years	2 (1.2%)	0	0	0	0
>= 75 years	0	.	0	.	0
Faeces soft (軟便)					
< 65 years	1 (0.9%)	0	0	0	0
>= 65 years	1 (1.3%)	0	0	0	0
< 75 years	2 (1.2%)	0	0	0	0
>= 75 years	0	.	0	.	0
Stomatitis (口内炎)					
< 65 years	0	0	1 (1.0%)	1 (2.1%)	2 (1.0%)
>= 65 years	0	0	0	0	0
< 75 years	0	0	1 (0.6%)	1 (1.3%)	2 (0.6%)
>= 75 years	0	.	0	.	0
Abdominal pain lower (下腹部痛)					
< 65 years	0	0	0	0	0
>= 65 years	1 (1.3%)	0	0	0	0
< 75 years	1 (0.6%)	0	0	0	0
>= 75 years	0	.	0	.	0
Abnormal faeces (異常便)					
< 65 years	0	0	0	0	0
>= 65 years	0	0	1 (1.2%)	0	1 (0.8%)
< 75 years	0	0	1 (0.6%)	0	1 (0.3%)
>= 75 years	0	.	0	.	0
Duodenal polyp (十二指腸ポリープ)					
< 65 years	0	1 (1.9%)	0	0	1 (0.5%)
>= 65 years	0	0	0	0	0
< 75 years	0	1 (1.3%)	0	0	1 (0.3%)
>= 75 years	0	.	0	.	0
Duodenitis (十二指腸炎)					
< 65 years	0	1 (1.9%)	0	0	1 (0.5%)
>= 65 years	0	0	0	0	0
< 75 years	0	1 (1.3%)	0	0	1 (0.3%)
>= 75 years	0	.	0	.	0
Enteritis (小腸炎)					
< 65 years	0	0	0	1 (2.1%)	1 (0.5%)
>= 65 years	0	0	0	0	0
< 75 years	0	0	0	1 (1.3%)	1 (0.3%)
>= 75 years	0	.	0	.	0
Enterocolitis (腸炎)					
< 65 years	1 (0.9%)	0	0	0	0
>= 65 years	0	0	0	0	0
< 75 years	1 (0.6%)	0	0	0	0
>= 75 years	0	.	0	.	0
Epigastric discomfort (心窩部不快感)					
< 65 years	0	0	1 (1.0%)	0	1 (0.5%)
>= 65 years	0	0	0	0	0
< 75 years	0	0	1 (0.6%)	0	1 (0.3%)

System Organ Class Preferred Term Age	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
>= 75 years	0	.	0	.	0
Gastric polyps (胃ポリープ)					
< 65 years	0	0	0	0	0
>= 65 years	1 (1.3%)	0	0	0	0
< 75 years	1 (0.6%)	0	0	0	0
>= 75 years	0	.	0	.	0
Ileus (イレウス)					
< 65 years	0	0	1 (1.0%)	0	1 (0.5%)
>= 65 years	0	0	0	0	0
< 75 years	0	0	1 (0.6%)	0	1 (0.3%)
>= 75 years	0	.	0	.	0
Large intestine polyp (大腸ポリープ)					
< 65 years	0	0	0	0	0
>= 65 years	0	0	1 (1.2%)	0	1 (0.8%)
< 75 years	0	0	0	0	0
>= 75 years	0	.	1 (11.1%)	.	1 (11.1%)
Loose tooth (弛緩歯)					
< 65 years	0	0	0	0	0
>= 65 years	0	0	1 (1.2%)	0	1 (0.8%)
< 75 years	0	0	1 (0.6%)	0	1 (0.3%)
>= 75 years	0	.	0	.	0
Melaena (メレナ)					
< 65 years	1 (0.9%)	0	0	0	0
>= 65 years	0	0	0	0	0
< 75 years	1 (0.6%)	0	0	0	0
>= 75 years	0	.	0	.	0
Tooth loss (歯の脱落)					
< 65 years	1 (0.9%)	0	0	0	0
>= 65 years	0	0	0	0	0
< 75 years	1 (0.6%)	0	0	0	0
>= 75 years	0	.	0	.	0
Metabolism and nutrition disorders (代謝および栄養障害)					
< 65 years	15 (14.2%)	7 (13.0%)	7 (7.2%)	5 (10.6%)	19 (9.6%)
>= 65 years	6 (7.9%)	1 (4.8%)	2 (2.4%)	0	3 (2.3%)
< 75 years	20 (11.8%)	8 (10.7%)	9 (5.3%)	5 (6.7%)	22 (6.9%)
>= 75 years	1 (7.7%)	.	0	.	0
Hyperglycaemia (高血糖)					
< 65 years	11 (10.4%)	3 (5.6%)	1 (1.0%)	1 (2.1%)	5 (2.5%)
>= 65 years	5 (6.6%)	0	0	0	0
< 75 years	15 (8.9%)	3 (4.0%)	1 (0.6%)	1 (1.3%)	5 (1.6%)
>= 75 years	1 (7.7%)	.	0	.	0
Hypoglycaemia (低血糖)					
< 65 years	2 (1.9%)	4 (7.4%)	5 (5.2%)	4 (8.5%)	13 (6.6%)
>= 65 years	0	1 (4.8%)	0	0	1 (0.8%)

System Organ Class Preferred Term Age	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
< 75 years	2 (1.2%)	5 (6.7%)	5 (2.9%)	4 (5.3%)	14 (4.4%)
>= 75 years	0	.	0	.	0
Dyslipidaemia (脂質異常症)					
< 65 years	2 (1.9%)	0	1 (1.0%)	0	1 (0.5%)
>= 65 years	1 (1.3%)	0	1 (1.2%)	0	1 (0.8%)
< 75 years	3 (1.8%)	0	2 (1.2%)	0	2 (0.6%)
>= 75 years	0	.	0	.	0
Hyperuricaemia (高尿酸血症)					
< 65 years	1 (0.9%)	0	0	0	0
>= 65 years	0	0	1 (1.2%)	0	1 (0.8%)
< 75 years	1 (0.6%)	0	1 (0.6%)	0	1 (0.3%)
>= 75 years	0	.	0	.	0
Musculoskeletal and connective tissue disorders (筋骨格系および結合組織障害)					
< 65 years	12 (11.3%)	6 (11.1%)	5 (5.2%)	5 (10.6%)	16 (8.1%)
>= 65 years	5 (6.6%)	3 (14.3%)	6 (7.2%)	0	9 (6.8%)
< 75 years	17 (10.1%)	9 (12.0%)	9 (5.3%)	5 (6.7%)	23 (7.2%)
>= 75 years	0	.	2 (22.2%)	.	2 (22.2%)
Arthralgia (関節痛)					
< 65 years	3 (2.8%)	1 (1.9%)	1 (1.0%)	1 (2.1%)	3 (1.5%)
>= 65 years	1 (1.3%)	0	0	0	0
< 75 years	4 (2.4%)	1 (1.3%)	1 (0.6%)	1 (1.3%)	3 (0.9%)
>= 75 years	0	.	0	.	0
Back pain (背部痛)					
< 65 years	0	3 (5.6%)	1 (1.0%)	1 (2.1%)	5 (2.5%)
>= 65 years	0	1 (4.8%)	0	0	1 (0.8%)
< 75 years	0	4 (5.3%)	1 (0.6%)	1 (1.3%)	6 (1.9%)
>= 75 years	0	.	0	.	0
Muscle spasms (筋痙縮)					
< 65 years	3 (2.8%)	0	0	0	0
>= 65 years	0	0	3 (3.6%)	0	3 (2.3%)
< 75 years	3 (1.8%)	0	2 (1.2%)	0	2 (0.6%)
>= 75 years	0	.	1 (11.1%)	.	1 (11.1%)
Periarthritis (関節周囲炎)					
< 65 years	1 (0.9%)	0	0	0	0
>= 65 years	1 (1.3%)	0	1 (1.2%)	0	1 (0.8%)
< 75 years	2 (1.2%)	0	1 (0.6%)	0	1 (0.3%)
>= 75 years	0	.	0	.	0
Musculoskeletal pain (筋骨格痛)					
< 65 years	1 (0.9%)	0	0	1 (2.1%)	1 (0.5%)
>= 65 years	0	0	0	0	0
< 75 years	1 (0.6%)	0	0	1 (1.3%)	1 (0.3%)
>= 75 years	0	.	0	.	0
Musculoskeletal stiffness (筋骨格硬直)					

System Organ Class Preferred Term Age	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
< 65 years	1 (0.9%)	0	0	0	0
>= 65 years	0	1 (4.8%)	0	0	1 (0.8%)
< 75 years	1 (0.6%)	1 (1.3%)	0	0	1 (0.3%)
>= 75 years	0	.	0	.	0
Osteoarthritis (変形性関節症)					
< 65 years	1 (0.9%)	0	0	0	0
>= 65 years	0	0	1 (1.2%)	0	1 (0.8%)
< 75 years	1 (0.6%)	0	1 (0.6%)	0	1 (0.3%)
>= 75 years	0	.	0	.	0
Plantar fasciitis (足底筋膜炎)					
< 65 years	1 (0.9%)	0	0	0	0
>= 65 years	1 (1.3%)	0	0	0	0
< 75 years	2 (1.2%)	0	0	0	0
>= 75 years	0	.	0	.	0
Arthritis (関節炎)					
< 65 years	0	1 (1.9%)	0	0	1 (0.5%)
>= 65 years	0	0	0	0	0
< 75 years	0	1 (1.3%)	0	0	1 (0.3%)
>= 75 years	0	.	0	.	0
Fasciitis (筋膜炎)					
< 65 years	0	0	0	0	0
>= 65 years	1 (1.3%)	0	0	0	0
< 75 years	1 (0.6%)	0	0	0	0
>= 75 years	0	.	0	.	0
Intervertebral disc degeneration (椎間板変性症)					
< 65 years	0	0	1 (1.0%)	0	1 (0.5%)
>= 65 years	0	0	0	0	0
< 75 years	0	0	1 (0.6%)	0	1 (0.3%)
>= 75 years	0	.	0	.	0
Intervertebral disc protrusion (椎間板突出)					
< 65 years	0	1 (1.9%)	0	0	1 (0.5%)
>= 65 years	0	0	0	0	0
< 75 years	0	1 (1.3%)	0	0	1 (0.3%)
>= 75 years	0	.	0	.	0
Joint swelling (関節腫脹)					
< 65 years	1 (0.9%)	0	0	0	0
>= 65 years	0	0	0	0	0
< 75 years	1 (0.6%)	0	0	0	0
>= 75 years	0	.	0	.	0
Mastication disorder (咀嚼障害)					
< 65 years	0	0	0	1 (2.1%)	1 (0.5%)
>= 65 years	0	0	0	0	0
< 75 years	0	0	0	1 (1.3%)	1 (0.3%)
>= 75 years	0	.	0	.	0

System Organ Class Preferred Term Age	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
Muscular weakness (筋力低下)					
< 65 years	0	0	1 (1.0%)	0	1 (0.5%)
>= 65 years	0	0	0	0	0
< 75 years	0	0	1 (0.6%)	0	1 (0.3%)
>= 75 years	0	.	0	.	0
Musculoskeletal chest pain (筋骨格系胸痛)					
< 65 years	0	1 (1.9%)	0	0	1 (0.5%)
>= 65 years	0	0	0	0	0
< 75 years	0	1 (1.3%)	0	0	1 (0.3%)
>= 75 years	0	.	0	.	0
Myalgia (筋肉痛)					
< 65 years	0	0	0	0	0
>= 65 years	0	0	1 (1.2%)	0	1 (0.8%)
< 75 years	0	0	0	0	0
>= 75 years	0	.	1 (11.1%)	.	1 (11.1%)
Neck pain (頚部痛)					
< 65 years	0	0	0	1 (2.1%)	1 (0.5%)
>= 65 years	0	0	0	0	0
< 75 years	0	0	0	1 (1.3%)	1 (0.3%)
>= 75 years	0	.	0	.	0
Osteoporosis (骨粗鬆症)					
< 65 years	0	0	0	0	0
>= 65 years	1 (1.3%)	0	0	0	0
< 75 years	1 (0.6%)	0	0	0	0
>= 75 years	0	.	0	.	0
Pain in extremity (四肢痛)					
< 65 years	0	0	0	0	0
>= 65 years	0	1 (4.8%)	0	0	1 (0.8%)
< 75 years	0	1 (1.3%)	0	0	1 (0.3%)
>= 75 years	0	.	0	.	0
Spinal osteoarthritis (変形性脊椎症)					
< 65 years	0	0	1 (1.0%)	0	1 (0.5%)
>= 65 years	0	0	0	0	0
< 75 years	0	0	1 (0.6%)	0	1 (0.3%)
>= 75 years	0	.	0	.	0
Spondylolisthesis (脊椎すべり症)					
< 65 years	1 (0.9%)	0	0	0	0
>= 65 years	0	0	0	0	0
< 75 years	1 (0.6%)	0	0	0	0
>= 75 years	0	.	0	.	0
Temporomandibular joint syndrome (顎関節症候群)					
< 65 years	0	0	0	1 (2.1%)	1 (0.5%)
>= 65 years	0	0	0	0	0
< 75 years	0	0	0	1 (1.3%)	1 (0.3%)

System Organ Class Preferred Term Age	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
>= 75 years	0	.	0	.	0
Injury, poisoning and procedural complications (傷害、中毒および処置合併症)					
< 65 years	3 (2.8%)	3 (5.6%)	3 (3.1%)	5 (10.6%)	11 (5.6%)
>= 65 years	3 (3.9%)	2 (9.5%)	5 (6.0%)	1 (3.6%)	8 (6.1%)
< 75 years	6 (3.6%)	5 (6.7%)	7 (4.1%)	6 (8.0%)	18 (5.6%)
>= 75 years	0	.	1 (11.1%)	.	1 (11.1%)
Contusion (挫傷)					
< 65 years	1 (0.9%)	2 (3.7%)	0	0	2 (1.0%)
>= 65 years	0	0	1 (1.2%)	1 (3.6%)	2 (1.5%)
< 75 years	1 (0.6%)	2 (2.7%)	1 (0.6%)	1 (1.3%)	4 (1.2%)
>= 75 years	0	.	0	.	0
Arthropod sting (節足動物刺傷)					
< 65 years	0	1 (1.9%)	0	2 (4.3%)	3 (1.5%)
>= 65 years	0	1 (4.8%)	0	0	1 (0.8%)
< 75 years	0	2 (2.7%)	0	2 (2.7%)	4 (1.2%)
>= 75 years	0	.	0	.	0
Hand fracture (手骨折)					
< 65 years	0	1 (1.9%)	0	0	1 (0.5%)
>= 65 years	0	0	0	1 (3.6%)	1 (0.8%)
< 75 years	0	1 (1.3%)	0	1 (1.3%)	2 (0.6%)
>= 75 years	0	.	0	.	0
Ligament sprain (靱帯捻挫)					
< 65 years	0	0	1 (1.0%)	1 (2.1%)	2 (1.0%)
>= 65 years	0	0	0	0	0
< 75 years	0	0	1 (0.6%)	1 (1.3%)	2 (0.6%)
>= 75 years	0	.	0	.	0
Radius fracture (橈骨骨折)					
< 65 years	0	0	0	1 (2.1%)	1 (0.5%)
>= 65 years	0	0	1 (1.2%)	0	1 (0.8%)
< 75 years	0	0	0	1 (1.3%)	1 (0.3%)
>= 75 years	0	.	1 (11.1%)	.	1 (11.1%)
Skin abrasion (皮膚擦過傷)					
< 65 years	0	0	1 (1.0%)	0	1 (0.5%)
>= 65 years	0	0	1 (1.2%)	0	1 (0.8%)
< 75 years	0	0	2 (1.2%)	0	2 (0.6%)
>= 75 years	0	.	0	.	0
Arthropod bite (節足動物咬傷)					
< 65 years	1 (0.9%)	0	0	0	0
>= 65 years	0	0	0	0	0
< 75 years	1 (0.6%)	0	0	0	0
>= 75 years	0	.	0	.	0
Bone contusion (骨挫傷)					
< 65 years	0	0	0	1 (2.1%)	1 (0.5%)

System Organ Class Preferred Term Age	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
>= 65 years	0	0	0	0	0
< 75 years	0	0	0	1 (1.3%)	1 (0.3%)
>= 75 years	0	.	0	.	0
Clavicle fracture (鎖骨骨折)					
< 65 years	0	0	0	0	0
>= 65 years	0	0	1 (1.2%)	0	1 (0.8%)
< 75 years	0	0	1 (0.6%)	0	1 (0.3%)
>= 75 years	0	.	0	.	0
Fall (転倒)					
< 65 years	0	0	0	0	0
>= 65 years	0	0	0	1 (3.6%)	1 (0.8%)
< 75 years	0	0	0	1 (1.3%)	1 (0.3%)
>= 75 years	0	.	0	.	0
Femur fracture (大腿骨骨折)					
< 65 years	0	0	0	0	0
>= 65 years	0	0	1 (1.2%)	0	1 (0.8%)
< 75 years	0	0	0	0	0
>= 75 years	0	.	1 (11.1%)	.	1 (11.1%)
Limb injury (四肢損傷)					
< 65 years	0	0	0	0	0
>= 65 years	1 (1.3%)	0	0	0	0
< 75 years	1 (0.6%)	0	0	0	0
>= 75 years	0	.	0	.	0
Lower limb fracture (下肢骨折)					
< 65 years	0	0	0	0	0
>= 65 years	1 (1.3%)	0	0	0	0
< 75 years	1 (0.6%)	0	0	0	0
>= 75 years	0	.	0	.	0
Meniscus injury (半月板損傷)					
< 65 years	1 (0.9%)	0	0	0	0
>= 65 years	0	0	0	0	0
< 75 years	1 (0.6%)	0	0	0	0
>= 75 years	0	.	0	.	0
Muscle rupture (筋断裂)					
< 65 years	0	0	0	0	0
>= 65 years	1 (1.3%)	0	0	0	0
< 75 years	1 (0.6%)	0	0	0	0
>= 75 years	0	.	0	.	0
Post procedural haemorrhage (処置後出血)					
< 65 years	0	0	0	0	0
>= 65 years	0	0	1 (1.2%)	0	1 (0.8%)
< 75 years	0	0	1 (0.6%)	0	1 (0.3%)
>= 75 years	0	.	0	.	0
Rib fracture (肋骨骨折)					
< 65 years	0	0	0	0	0

System Organ Class Preferred Term Age	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
>= 65 years	0	1 (4.8%)	0	0	1 (0.8%)
< 75 years	0	1 (1.3%)	0	0	1 (0.3%)
>= 75 years	0	.	0	.	0
Thermal burn (熱傷)					
< 65 years	0	0	1 (1.0%)	0	1 (0.5%)
>= 65 years	0	0	0	0	0
< 75 years	0	0	1 (0.6%)	0	1 (0.3%)
>= 75 years	0	.	0	.	0
Skin and subcutaneous tissue disorders (皮膚および皮下組織障害)					
< 65 years	7 (6.6%)	1 (1.9%)	2 (2.1%)	4 (8.5%)	7 (3.5%)
>= 65 years	5 (6.6%)	2 (9.5%)	3 (3.6%)	1 (3.6%)	6 (4.5%)
< 75 years	10 (5.9%)	3 (4.0%)	5 (2.9%)	5 (6.7%)	13 (4.0%)
>= 75 years	2 (15.4%)	.	0	.	0
Eczema (湿疹)					
< 65 years	2 (1.9%)	0	2 (2.1%)	2 (4.3%)	4 (2.0%)
>= 65 years	0	2 (9.5%)	0	1 (3.6%)	3 (2.3%)
< 75 years	2 (1.2%)	2 (2.7%)	2 (1.2%)	3 (4.0%)	7 (2.2%)
>= 75 years	0	.	0	.	0
Dermatitis contact (接触皮膚炎)					
< 65 years	0	0	0	0	0
>= 65 years	1 (1.3%)	0	1 (1.2%)	0	1 (0.8%)
< 75 years	0	0	1 (0.6%)	0	1 (0.3%)
>= 75 years	1 (7.7%)	.	0	.	0
Dyshidrotic eczema (異汗性湿疹)					
< 65 years	1 (0.9%)	0	0	0	0
>= 65 years	0	0	1 (1.2%)	0	1 (0.8%)
< 75 years	1 (0.6%)	0	1 (0.6%)	0	1 (0.3%)
>= 75 years	0	.	0	.	0
Ingrowing nail (嵌入爪)					
< 65 years	0	0	0	1 (2.1%)	1 (0.5%)
>= 65 years	1 (1.3%)	0	0	0	0
< 75 years	1 (0.6%)	0	0	1 (1.3%)	1 (0.3%)
>= 75 years	0	.	0	.	0
Miliaria (汗疹)					
< 65 years	1 (0.9%)	1 (1.9%)	0	0	1 (0.5%)
>= 65 years	0	0	0	0	0
< 75 years	1 (0.6%)	1 (1.3%)	0	0	1 (0.3%)
>= 75 years	0	.	0	.	0
Alopecia areata (円形脱毛症)					
< 65 years	1 (0.9%)	0	0	0	0
>= 65 years	0	0	0	0	0
< 75 years	1 (0.6%)	0	0	0	0
>= 75 years	0	.	0	.	0
Drug eruption (薬疹)					

System Organ Class Preferred Term Age	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
< 65 years	1 (0.9%)	0	0	0	0
>= 65 years	0	0	0	0	0
< 75 years	1 (0.6%)	0	0	0	0
>= 75 years	0	.	0	.	0
Dry skin (皮膚乾燥)					
< 65 years	0	0	0	0	0
>= 65 years	0	0	1 (1.2%)	0	1 (0.8%)
< 75 years	0	0	1 (0.6%)	0	1 (0.3%)
>= 75 years	0	.	0	.	0
Eczema asteatotic (皮脂欠乏性湿疹)					
< 65 years	0	0	0	0	0
>= 65 years	1 (1.3%)	0	0	0	0
< 75 years	1 (0.6%)	0	0	0	0
>= 75 years	0	.	0	.	0
Pruritus (そう痒症)					
< 65 years	1 (0.9%)	0	0	0	0
>= 65 years	0	0	0	0	0
< 75 years	1 (0.6%)	0	0	0	0
>= 75 years	0	.	0	.	0
Pustular psoriasis (膿疱性乾癬)					
< 65 years	1 (0.9%)	0	0	0	0
>= 65 years	0	0	0	0	0
< 75 years	1 (0.6%)	0	0	0	0
>= 75 years	0	.	0	.	0
Rash (発疹)					
< 65 years	0	0	0	0	0
>= 65 years	1 (1.3%)	0	0	0	0
< 75 years	1 (0.6%)	0	0	0	0
>= 75 years	0	.	0	.	0
Toxic skin eruption (中毒性皮疹)					
< 65 years	0	0	0	0	0
>= 65 years	1 (1.3%)	0	0	0	0
< 75 years	1 (0.6%)	0	0	0	0
>= 75 years	0	.	0	.	0
Urticaria (蕁麻疹)					
< 65 years	0	0	0	0	0
>= 65 years	1 (1.3%)	0	0	0	0
< 75 years	0	0	0	0	0
>= 75 years	1 (7.7%)	.	0	.	0
Xanthoma (黄色腫)					
< 65 years	0	0	0	1 (2.1%)	1 (0.5%)
>= 65 years	0	0	0	0	0
< 75 years	0	0	0	1 (1.3%)	1 (0.3%)
>= 75 years	0	.	0	.	0

Nervous system disorders (神経系障害)

System Organ Class Preferred Term Age	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
< 65 years	6 (5.7%)	4 (7.4%)	4 (4.1%)	1 (2.1%)	9 (4.5%)
>= 65 years	4 (5.3%)	2 (9.5%)	3 (3.6%)	0	5 (3.8%)
< 75 years	10 (5.9%)	6 (8.0%)	7 (4.1%)	1 (1.3%)	14 (4.4%)
>= 75 years	0	.	0	.	0
Dizziness (浮動性めまい)					
< 65 years	3 (2.8%)	1 (1.9%)	0	0	1 (0.5%)
>= 65 years	1 (1.3%)	0	1 (1.2%)	0	1 (0.8%)
< 75 years	4 (2.4%)	1 (1.3%)	1 (0.6%)	0	2 (0.6%)
>= 75 years	0	.	0	.	0
Headache (頭痛)					
< 65 years	2 (1.9%)	2 (3.7%)	1 (1.0%)	0	3 (1.5%)
>= 65 years	0	0	0	0	0
< 75 years	2 (1.2%)	2 (2.7%)	1 (0.6%)	0	3 (0.9%)
>= 75 years	0	.	0	.	0
Cervical radiculopathy (頚髄神経根障害)					
< 65 years	0	0	0	0	0
>= 65 years	1 (1.3%)	0	1 (1.2%)	0	1 (0.8%)
< 75 years	1 (0.6%)	0	1 (0.6%)	0	1 (0.3%)
>= 75 years	0	.	0	.	0
Dizziness postural (体位性めまい)					
< 65 years	1 (0.9%)	1 (1.9%)	0	0	1 (0.5%)
>= 65 years	0	0	0	0	0
< 75 years	1 (0.6%)	1 (1.3%)	0	0	1 (0.3%)
>= 75 years	0	.	0	.	0
Presyncope (失神寸前の状態)					
< 65 years	0	0	1 (1.0%)	0	1 (0.5%)
>= 65 years	0	0	1 (1.2%)	0	1 (0.8%)
< 75 years	0	0	2 (1.2%)	0	2 (0.6%)
>= 75 years	0	.	0	.	0
Carpal tunnel syndrome (手根管症候群)					
< 65 years	0	0	1 (1.0%)	0	1 (0.5%)
>= 65 years	0	0	0	0	0
< 75 years	0	0	1 (0.6%)	0	1 (0.3%)
>= 75 years	0	.	0	.	0
Dysgeusia (味覚異常)					
< 65 years	0	0	0	1 (2.1%)	1 (0.5%)
>= 65 years	0	0	0	0	0
< 75 years	0	0	0	1 (1.3%)	1 (0.3%)
>= 75 years	0	.	0	.	0
Hypoaesthesia (感覚鈍麻)					
< 65 years	0	0	0	0	0
>= 65 years	1 (1.3%)	0	0	0	0
< 75 years	1 (0.6%)	0	0	0	0
>= 75 years	0	.	0	.	0

System Organ Class Preferred Term Age	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
IVth nerve disorder (第 4 脳神経障害)					
< 65 years	0	0	0	0	0
>= 65 years	0	1 (4.8%)	0	0	1 (0.8%)
< 75 years	0	1 (1.3%)	0	0	1 (0.3%)
>= 75 years	0	.	0	.	0
Intercostal neuralgia (肋間神経痛)					
< 65 years	0	0	0	0	0
>= 65 years	1 (1.3%)	0	0	0	0
< 75 years	1 (0.6%)	0	0	0	0
>= 75 years	0	.	0	.	0
Loss of consciousness (意識消失)					
< 65 years	0	0	0	0	0
>= 65 years	0	0	1 (1.2%)	0	1 (0.8%)
< 75 years	0	0	1 (0.6%)	0	1 (0.3%)
>= 75 years	0	.	0	.	0
Orthostatic intolerance (起立不耐性)					
< 65 years	0	0	0	0	0
>= 65 years	0	1 (4.8%)	0	0	1 (0.8%)
< 75 years	0	1 (1.3%)	0	0	1 (0.3%)
>= 75 years	0	.	0	.	0
Spondylitic myelopathy (脊椎炎性脊髄症)					
< 65 years	0	0	1 (1.0%)	0	1 (0.5%)
>= 65 years	0	0	0	0	0
< 75 years	0	0	1 (0.6%)	0	1 (0.3%)
>= 75 years	0	.	0	.	0
Thoracic outlet syndrome (胸郭出口症候群)					
< 65 years	0	1 (1.9%)	0	0	1 (0.5%)
>= 65 years	0	0	0	0	0
< 75 years	0	1 (1.3%)	0	0	1 (0.3%)
>= 75 years	0	.	0	.	0
Investigations (臨床検査)					
< 65 years	5 (4.7%)	4 (7.4%)	2 (2.1%)	4 (8.5%)	10 (5.1%)
>= 65 years	2 (2.6%)	1 (4.8%)	2 (2.4%)	2 (7.1%)	5 (3.8%)
< 75 years	7 (4.1%)	5 (6.7%)	4 (2.3%)	6 (8.0%)	15 (4.7%)
>= 75 years	0	.	0	.	0
Culture urine positive (尿培養陽性)					
< 65 years	1 (0.9%)	0	0	3 (6.4%)	3 (1.5%)
>= 65 years	0	1 (4.8%)	0	1 (3.6%)	2 (1.5%)
< 75 years	1 (0.6%)	1 (1.3%)	0	4 (5.3%)	5 (1.6%)
>= 75 years	0	.	0	.	0
Blood bilirubin increased (血中ビリルビン増加)					
< 65 years	1 (0.9%)	0	0	0	0

System Organ Class Preferred Term Age	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
>= 65 years	1 (1.3%)	0	0	0	0
< 75 years	2 (1.2%)	0	0	0	0
>= 75 years	0	.	0	.	0
Blood creatine phosphokinase increased (血中クレアチンホスホキナーゼ増加)					
< 65 years	2 (1.9%)	0	0	0	0
>= 65 years	0	0	0	0	0
< 75 years	2 (1.2%)	0	0	0	0
>= 75 years	0	.	0	.	0
Gamma-glutamyltransferase increased (γ－グルタミルトランスフェラーゼ増加)					
< 65 years	1 (0.9%)	0	0	0	0
>= 65 years	0	0	0	1 (3.6%)	1 (0.8%)
< 75 years	1 (0.6%)	0	0	1 (1.3%)	1 (0.3%)
>= 75 years	0	.	0	.	0
Urine albumin/creatinine ratio increased (尿中アルブミン／クレアチニン比増加)					
< 65 years	0	0	1 (1.0%)	0	1 (0.5%)
>= 65 years	1 (1.3%)	0	0	0	0
< 75 years	1 (0.6%)	0	1 (0.6%)	0	1 (0.3%)
>= 75 years	0	.	0	.	0
Activated partial thromboplastin time prolonged (活性化部分トロンボプラスチン時間延長)					
< 65 years	0	1 (1.9%)	0	0	1 (0.5%)
>= 65 years	0	0	0	0	0
< 75 years	0	1 (1.3%)	0	0	1 (0.3%)
>= 75 years	0	.	0	.	0
Alanine aminotransferase increased (アラニンアミノトランスフェラーゼ増加)					
< 65 years	1 (0.9%)	0	0	0	0
>= 65 years	0	0	0	0	0
< 75 years	1 (0.6%)	0	0	0	0
>= 75 years	0	.	0	.	0
Aspartate aminotransferase increased (アスパラギン酸アミノトランスフェラーゼ増加)					
< 65 years	1 (0.9%)	0	0	0	0
>= 65 years	0	0	0	0	0
< 75 years	1 (0.6%)	0	0	0	0
>= 75 years	0	.	0	.	0
Blood glucagon increased (血中グルカゴン増加)					
< 65 years	0	0	0	1 (2.1%)	1 (0.5%)

System Organ Class Preferred Term Age	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
>= 65 years	0	0	0	0	0
< 75 years	0	0	0	1 (1.3%)	1 (0.3%)
>= 75 years	0	.	0	.	0
Blood pressure increased (血圧上昇)					
< 65 years	1 (0.9%)	0	0	0	0
>= 65 years	0	0	0	0	0
< 75 years	1 (0.6%)	0	0	0	0
>= 75 years	0	.	0	.	0
C-reactive protein increased (Ｃ－反応性蛋白増加)					
< 65 years	0	0	0	0	0
>= 65 years	0	0	1 (1.2%)	0	1 (0.8%)
< 75 years	0	0	1 (0.6%)	0	1 (0.3%)
>= 75 years	0	.	0	.	0
Electrocardiogram T wave inversion (心電図Ｔ波逆転)					
< 65 years	0	0	0	1 (2.1%)	1 (0.5%)
>= 65 years	0	0	0	0	0
< 75 years	0	0	0	1 (1.3%)	1 (0.3%)
>= 75 years	0	.	0	.	0
Eosinophil count increased (好酸球数増加)					
< 65 years	0	1 (1.9%)	0	0	1 (0.5%)
>= 65 years	0	0	0	0	0
< 75 years	0	1 (1.3%)	0	0	1 (0.3%)
>= 75 years	0	.	0	.	0
International normalised ratio increased (国際標準比増加)					
< 65 years	0	1 (1.9%)	0	0	1 (0.5%)
>= 65 years	0	0	0	0	0
< 75 years	0	1 (1.3%)	0	0	1 (0.3%)
>= 75 years	0	.	0	.	0
Lipase increased (リパーゼ増加)					
< 65 years	0	1 (1.9%)	0	0	1 (0.5%)
>= 65 years	0	0	0	0	0
< 75 years	0	1 (1.3%)	0	0	1 (0.3%)
>= 75 years	0	.	0	.	0
Liver function test increased (肝機能検査値上昇)					
< 65 years	0	0	1 (1.0%)	0	1 (0.5%)
>= 65 years	0	0	0	0	0
< 75 years	0	0	1 (0.6%)	0	1 (0.3%)
>= 75 years	0	.	0	.	0
Neutrophil count decreased (好中球数減少)					
< 65 years	0	0	0	0	0

System Organ Class Preferred Term Age	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
>= 65 years	0	0	1 (1.2%)	0	1 (0.8%)
< 75 years	0	0	1 (0.6%)	0	1 (0.3%)
>= 75 years	0	.	0	.	0
Occult blood (便潜血)					
< 65 years	0	1 (1.9%)	0	0	1 (0.5%)
>= 65 years	0	0	0	0	0
< 75 years	0	1 (1.3%)	0	0	1 (0.3%)
>= 75 years	0	.	0	.	0
General disorders and administration site conditions (一般・全身障害および投与部位の状態)					
< 65 years	4 (3.8%)	0	1 (1.0%)	2 (4.3%)	3 (1.5%)
>= 65 years	1 (1.3%)	1 (4.8%)	3 (3.6%)	3 (10.7%)	7 (5.3%)
< 75 years	5 (3.0%)	1 (1.3%)	3 (1.8%)	5 (6.7%)	9 (2.8%)
>= 75 years	0	.	1 (11.1%)	.	1 (11.1%)
Fatigue (疲労)					
< 65 years	1 (0.9%)	0	0	0	0
>= 65 years	0	0	2 (2.4%)	2 (7.1%)	4 (3.0%)
< 75 years	1 (0.6%)	0	1 (0.6%)	2 (2.7%)	3 (0.9%)
>= 75 years	0	.	1 (11.1%)	.	1 (11.1%)
Malaise (倦怠感)					
< 65 years	1 (0.9%)	0	0	0	0
>= 65 years	0	1 (4.8%)	1 (1.2%)	1 (3.6%)	3 (2.3%)
< 75 years	1 (0.6%)	1 (1.3%)	1 (0.6%)	1 (1.3%)	3 (0.9%)
>= 75 years	0	.	0	.	0
Pyrexia (発熱)					
< 65 years	1 (0.9%)	0	0	0	0
>= 65 years	1 (1.3%)	0	0	0	0
< 75 years	2 (1.2%)	0	0	0	0
>= 75 years	0	.	0	.	0
Chest discomfort (胸部不快感)					
< 65 years	0	0	1 (1.0%)	0	1 (0.5%)
>= 65 years	0	0	0	0	0
< 75 years	0	0	1 (0.6%)	0	1 (0.3%)
>= 75 years	0	.	0	.	0
Feeling abnormal (異常感)					
< 65 years	0	0	0	1 (2.1%)	1 (0.5%)
>= 65 years	0	0	0	0	0
< 75 years	0	0	0	1 (1.3%)	1 (0.3%)
>= 75 years	0	.	0	.	0
Oedema peripheral (末梢性浮腫)					
< 65 years	0	0	0	1 (2.1%)	1 (0.5%)
>= 65 years	0	0	0	0	0
< 75 years	0	0	0	1 (1.3%)	1 (0.3%)
>= 75 years	0	.	0	.	0

System Organ Class Preferred Term Age	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
Thirst (口渇)					
< 65 years	1 (0.9%)	0	0	0	0
>= 65 years	0	0	0	0	0
< 75 years	1 (0.6%)	0	0	0	0
>= 75 years	0	.	0	.	0
Eye disorders (眼障害)					
< 65 years	3 (2.8%)	2 (3.7%)	0	2 (4.3%)	4 (2.0%)
>= 65 years	1 (1.3%)	0	4 (4.8%)	1 (3.6%)	5 (3.8%)
< 75 years	3 (1.8%)	2 (2.7%)	3 (1.8%)	3 (4.0%)	8 (2.5%)
>= 75 years	1 (7.7%)	.	1 (11.1%)	.	1 (11.1%)
Cataract (白内障)					
< 65 years	1 (0.9%)	0	0	0	0
>= 65 years	0	0	0	1 (3.6%)	1 (0.8%)
< 75 years	1 (0.6%)	0	0	1 (1.3%)	1 (0.3%)
>= 75 years	0	.	0	.	0
Chalazion (霰粒腫)					
< 65 years	0	1 (1.9%)	0	1 (2.1%)	2 (1.0%)
>= 65 years	0	0	0	0	0
< 75 years	0	1 (1.3%)	0	1 (1.3%)	2 (0.6%)
>= 75 years	0	.	0	.	0
Diabetic retinopathy (糖尿病網膜症)					
< 65 years	0	0	0	0	0
>= 65 years	0	0	2 (2.4%)	0	2 (1.5%)
< 75 years	0	0	1 (0.6%)	0	1 (0.3%)
>= 75 years	0	.	1 (11.1%)	.	1 (11.1%)
Glaucoma (緑内障)					
< 65 years	0	0	0	0	0
>= 65 years	0	0	2 (2.4%)	0	2 (1.5%)
< 75 years	0	0	1 (0.6%)	0	1 (0.3%)
>= 75 years	0	.	1 (11.1%)	.	1 (11.1%)
Vitreous floaters (硝子体浮遊物)					
< 65 years	2 (1.9%)	0	0	0	0
>= 65 years	0	0	0	0	0
< 75 years	2 (1.2%)	0	0	0	0
>= 75 years	0	.	0	.	0
Dry eye (眼乾燥)					
< 65 years	0	0	0	0	0
>= 65 years	1 (1.3%)	0	0	0	0
< 75 years	0	0	0	0	0
>= 75 years	1 (7.7%)	.	0	.	0
Eye inflammation (眼の炎症)					
< 65 years	0	0	0	1 (2.1%)	1 (0.5%)
>= 65 years	0	0	0	0	0
< 75 years	0	0	0	1 (1.3%)	1 (0.3%)
>= 75 years	0	.	0	.	0

System Organ Class Preferred Term Age	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
Eye swelling (眼部腫脹)					
< 65 years	0	1 (1.9%)	0	0	1 (0.5%)
>= 65 years	0	0	0	0	0
< 75 years	0	1 (1.3%)	0	0	1 (0.3%)
>= 75 years	0	.	0	.	0
Macular fibrosis (黄斑線維症)					
< 65 years	0	0	0	0	0
>= 65 years	0	0	1 (1.2%)	0	1 (0.8%)
< 75 years	0	0	1 (0.6%)	0	1 (0.3%)
>= 75 years	0	.	0	.	0
Respiratory, thoracic and mediastinal disorders (呼吸器、胸郭および縦隔障害)					
< 65 years	4 (3.8%)	3 (5.6%)	0	1 (2.1%)	4 (2.0%)
>= 65 years	0	0	0	1 (3.6%)	1 (0.8%)
< 75 years	4 (2.4%)	3 (4.0%)	0	2 (2.7%)	5 (1.6%)
>= 75 years	0	.	0	.	0
Oropharyngeal pain (口腔咽頭痛)					
< 65 years	1 (0.9%)	0	0	1 (2.1%)	1 (0.5%)
>= 65 years	0	0	0	1 (3.6%)	1 (0.8%)
< 75 years	1 (0.6%)	0	0	2 (2.7%)	2 (0.6%)
>= 75 years	0	.	0	.	0
Upper respiratory tract inflammation (上気道の炎症)					
< 65 years	2 (1.9%)	1 (1.9%)	0	0	1 (0.5%)
>= 65 years	0	0	0	0	0
< 75 years	2 (1.2%)	1 (1.3%)	0	0	1 (0.3%)
>= 75 years	0	.	0	.	0
Rhinitis allergic (アレルギー性鼻炎)					
< 65 years	0	2 (3.7%)	0	0	2 (1.0%)
>= 65 years	0	0	0	0	0
< 75 years	0	2 (2.7%)	0	0	2 (0.6%)
>= 75 years	0	.	0	.	0
Allergic cough (アレルギー性咳嗽)					
< 65 years	1 (0.9%)	0	0	0	0
>= 65 years	0	0	0	0	0
< 75 years	1 (0.6%)	0	0	0	0
>= 75 years	0	.	0	.	0
Asthma (喘息)					
< 65 years	1 (0.9%)	0	0	0	0
>= 65 years	0	0	0	0	0
< 75 years	1 (0.6%)	0	0	0	0
>= 75 years	0	.	0	.	0
Cardiac disorders (心臓障害)					
< 65 years	2 (1.9%)	0	1 (1.0%)	1 (2.1%)	2 (1.0%)

System Organ Class Preferred Term Age	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
>= 65 years	0	0	1 (1.2%)	2 (7.1%)	3 (2.3%)
< 75 years	2 (1.2%)	0	2 (1.2%)	3 (4.0%)	5 (1.6%)
>= 75 years	0	.	0	.	0
Palpitations (動悸)					
< 65 years	2 (1.9%)	0	1 (1.0%)	1 (2.1%)	2 (1.0%)
>= 65 years	0	0	0	0	0
< 75 years	2 (1.2%)	0	1 (0.6%)	1 (1.3%)	2 (0.6%)
>= 75 years	0	.	0	.	0
Atrial fibrillation (心房細動)					
< 65 years	0	0	0	0	0
>= 65 years	0	0	0	1 (3.6%)	1 (0.8%)
< 75 years	0	0	0	1 (1.3%)	1 (0.3%)
>= 75 years	0	.	0	.	0
Bradycardia (徐脈)					
< 65 years	0	0	0	0	0
>= 65 years	0	0	1 (1.2%)	0	1 (0.8%)
< 75 years	0	0	1 (0.6%)	0	1 (0.3%)
>= 75 years	0	.	0	.	0
Ventricular extrasystoles (心室性期外収縮)					
< 65 years	0	0	0	0	0
>= 65 years	0	0	0	1 (3.6%)	1 (0.8%)
< 75 years	0	0	0	1 (1.3%)	1 (0.3%)
>= 75 years	0	.	0	.	0
Vascular disorders (血管障害)					
< 65 years	3 (2.8%)	2 (3.7%)	0	0	2 (1.0%)
>= 65 years	0	0	1 (1.2%)	1 (3.6%)	2 (1.5%)
< 75 years	3 (1.8%)	2 (2.7%)	1 (0.6%)	1 (1.3%)	4 (1.2%)
>= 75 years	0	.	0	.	0
Hypertension (高血圧)					
< 65 years	2 (1.9%)	2 (3.7%)	0	0	2 (1.0%)
>= 65 years	0	0	1 (1.2%)	1 (3.6%)	2 (1.5%)
< 75 years	2 (1.2%)	2 (2.7%)	1 (0.6%)	1 (1.3%)	4 (1.2%)
>= 75 years	0	.	0	.	0
Arteriosclerosis (動脈硬化症)					
< 65 years	1 (0.9%)	0	0	0	0
>= 65 years	0	0	0	0	0
< 75 years	1 (0.6%)	0	0	0	0
>= 75 years	0	.	0	.	0
Ear and labyrinth disorders (耳および迷路障害)					
< 65 years	1 (0.9%)	0	0	2 (4.3%)	2 (1.0%)
>= 65 years	0	0	2 (2.4%)	1 (3.6%)	3 (2.3%)
< 75 years	1 (0.6%)	0	2 (1.2%)	3 (4.0%)	5 (1.6%)

System Organ Class Preferred Term Age	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
>= 75 years	0	.	0	.	0
Vertigo (回転性めまい)					
< 65 years	0	0	0	1 (2.1%)	1 (0.5%)
>= 65 years	0	0	1 (1.2%)	1 (3.6%)	2 (1.5%)
< 75 years	0	0	1 (0.6%)	2 (2.7%)	3 (0.9%)
>= 75 years	0	.	0	.	0
Ear congestion (耳閉)					
< 65 years	0	0	0	1 (2.1%)	1 (0.5%)
>= 65 years	0	0	0	0	0
< 75 years	0	0	0	1 (1.3%)	1 (0.3%)
>= 75 years	0	.	0	.	0
Eustachian tube stenosis (耳管狭窄)					
< 65 years	1 (0.9%)	0	0	0	0
>= 65 years	0	0	0	0	0
< 75 years	1 (0.6%)	0	0	0	0
>= 75 years	0	.	0	.	0
Vertigo positional (頭位性回転性めまい)					
< 65 years	0	0	0	0	0
>= 65 years	0	0	1 (1.2%)	0	1 (0.8%)
< 75 years	0	0	1 (0.6%)	0	1 (0.3%)
>= 75 years	0	.	0	.	0
Hepatobiliary disorders (肝胆道系障害)					
< 65 years	1 (0.9%)	0	1 (1.0%)	2 (4.3%)	3 (1.5%)
>= 65 years	2 (2.6%)	0	0	0	0
< 75 years	3 (1.8%)	0	1 (0.6%)	2 (2.7%)	3 (0.9%)
>= 75 years	0	.	0	.	0
Hepatic steatosis (脂肪肝)					
< 65 years	0	0	0	1 (2.1%)	1 (0.5%)
>= 65 years	1 (1.3%)	0	0	0	0
< 75 years	1 (0.6%)	0	0	1 (1.3%)	1 (0.3%)
>= 75 years	0	.	0	.	0
Gallbladder polyp (胆嚢ポリープ)					
< 65 years	1 (0.9%)	0	0	0	0
>= 65 years	0	0	0	0	0
< 75 years	1 (0.6%)	0	0	0	0
>= 75 years	0	.	0	.	0
Hepatic function abnormal (肝機能異常)					
< 65 years	0	0	1 (1.0%)	0	1 (0.5%)
>= 65 years	0	0	0	0	0
< 75 years	0	0	1 (0.6%)	0	1 (0.3%)
>= 75 years	0	.	0	.	0
Hepatomegaly (肝腫大)					
< 65 years	0	0	0	1 (2.1%)	1 (0.5%)

System Organ Class Preferred Term Age	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
>= 65 years	0	0	0	0	0
< 75 years	0	0	0	1 (1.3%)	1 (0.3%)
>= 75 years	0	.	0	.	0
Liver injury (肝損傷)					
< 65 years	0	0	0	0	0
>= 65 years	1 (1.3%)	0	0	0	0
< 75 years	1 (0.6%)	0	0	0	0
>= 75 years	0	.	0	.	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps) (良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）)					
< 65 years	0	0	2 (2.1%)	0	2 (1.0%)
>= 65 years	0	0	2 (2.4%)	1 (3.6%)	3 (2.3%)
< 75 years	0	0	3 (1.8%)	1 (1.3%)	4 (1.2%)
>= 75 years	0	.	1 (11.1%)	.	1 (11.1%)
Bladder cancer (膀胱癌)					
< 65 years	0	0	0	0	0
>= 65 years	0	0	1 (1.2%)	0	1 (0.8%)
< 75 years	0	0	0	0	0
>= 75 years	0	.	1 (11.1%)	.	1 (11.1%)
Pancreatic carcinoma metastatic (遠隔転移を伴う膵癌)					
< 65 years	0	0	0	0	0
>= 65 years	0	0	0	1 (3.6%)	1 (0.8%)
< 75 years	0	0	0	1 (1.3%)	1 (0.3%)
>= 75 years	0	.	0	.	0
Prostate cancer (前立腺癌)					
< 65 years	0	0	0	0	0
>= 65 years	0	0	1 (1.2%)	0	1 (0.8%)
< 75 years	0	0	1 (0.6%)	0	1 (0.3%)
>= 75 years	0	.	0	.	0
Seborrhoeic keratosis (脂漏性角化症)					
< 65 years	0	0	1 (1.0%)	0	1 (0.5%)
>= 65 years	0	0	0	0	0
< 75 years	0	0	1 (0.6%)	0	1 (0.3%)
>= 75 years	0	.	0	.	0
Solid pseudopapillary tumour of the pancreas (膵の充実性偽乳頭状腫瘍)					
< 65 years	0	0	1 (1.0%)	0	1 (0.5%)
>= 65 years	0	0	0	0	0
< 75 years	0	0	1 (0.6%)	0	1 (0.3%)
>= 75 years	0	.	0	.	0
Psychiatric disorders (精神障害)					

System Organ Class Preferred Term Age	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
< 65 years	1 (0.9%)	0	0	0	0
>= 65 years	0	1 (4.8%)	0	1 (3.6%)	2 (1.5%)
< 75 years	1 (0.6%)	1 (1.3%)	0	1 (1.3%)	2 (0.6%)
>= 75 years	0	.	0	.	0
Insomnia (不眠症)					
< 65 years	0	0	0	0	0
>= 65 years	0	1 (4.8%)	0	1 (3.6%)	2 (1.5%)
< 75 years	0	1 (1.3%)	0	1 (1.3%)	2 (0.6%)
>= 75 years	0	.	0	.	0
Anxiety (不安)					
< 65 years	1 (0.9%)	0	0	0	0
>= 65 years	0	0	0	0	0
< 75 years	1 (0.6%)	0	0	0	0
>= 75 years	0	.	0	.	0
Renal and urinary disorders (腎および尿路障害)					
< 65 years	1 (0.9%)	1 (1.9%)	0	0	1 (0.5%)
>= 65 years	0	0	1 (1.2%)	0	1 (0.8%)
< 75 years	1 (0.6%)	1 (1.3%)	1 (0.6%)	0	2 (0.6%)
>= 75 years	0	.	0	.	0
Calculus urinary (尿路結石)					
< 65 years	1 (0.9%)	0	0	0	0
>= 65 years	0	0	0	0	0
< 75 years	1 (0.6%)	0	0	0	0
>= 75 years	0	.	0	.	0
Diabetic nephropathy (糖尿病性腎症)					
< 65 years	0	1 (1.9%)	0	0	1 (0.5%)
>= 65 years	0	0	0	0	0
< 75 years	0	1 (1.3%)	0	0	1 (0.3%)
>= 75 years	0	.	0	.	0
Ureterolithiasis (尿管結石症)					
< 65 years	0	0	0	0	0
>= 65 years	0	0	1 (1.2%)	0	1 (0.8%)
< 75 years	0	0	1 (0.6%)	0	1 (0.3%)
>= 75 years	0	.	0	.	0
Reproductive system and breast disorders (生殖系および乳房障害)					
< 65 years	1 (0.9%)	1 (1.9%)	0	0	1 (0.5%)
>= 65 years	1 (1.3%)	0	0	0	0
< 75 years	1 (0.6%)	1 (1.3%)	0	0	1 (0.3%)
>= 75 years	1 (7.7%)	.	0	.	0
Benign prostatic hyperplasia (良性前立腺肥大症)					
< 65 years	0	0	0	0	0

System Organ Class Preferred Term Age	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
>= 65 years	1 (1.3%)	0	0	0	0
< 75 years	0	0	0	0	0
>= 75 years	1 (7.7%)	.	0	.	0
Dysmenorrhoea (月経困難症)					
< 65 years	1 (0.9%)	0	0	0	0
>= 65 years	0	0	0	0	0
< 75 years	1 (0.6%)	0	0	0	0
>= 75 years	0	.	0	.	0
Metrorrhagia (不正子宮出血)					
< 65 years	0	1 (1.9%)	0	0	1 (0.5%)
>= 65 years	0	0	0	0	0
< 75 years	0	1 (1.3%)	0	0	1 (0.3%)
>= 75 years	0	.	0	.	0
Prostatitis (前立腺炎)					
< 65 years	0	0	0	0	0
>= 65 years	1 (1.3%)	0	0	0	0
< 75 years	0	0	0	0	0
>= 75 years	1 (7.7%)	.	0	.	0
Blood and lymphatic system disorders (血液およびリンパ系障害)					
< 65 years	0	0	1 (1.0%)	0	1 (0.5%)
>= 65 years	0	0	0	0	0
< 75 years	0	0	1 (0.6%)	0	1 (0.3%)
>= 75 years	0	.	0	.	0
Anaemia (貧血)					
< 65 years	0	0	1 (1.0%)	0	1 (0.5%)
>= 65 years	0	0	0	0	0
< 75 years	0	0	1 (0.6%)	0	1 (0.3%)
>= 75 years	0	.	0	.	0
Endocrine disorders (内分泌障害)					
< 65 years	0	0	0	1 (2.1%)	1 (0.5%)
>= 65 years	0	0	0	0	0
< 75 years	0	0	0	1 (1.3%)	1 (0.3%)
>= 75 years	0	.	0	.	0
Thyroid cyst (甲状腺嚢腫)					
< 65 years	0	0	0	1 (2.1%)	1 (0.5%)
>= 65 years	0	0	0	0	0
< 75 years	0	0	0	1 (1.3%)	1 (0.3%)
>= 75 years	0	.	0	.	0
Thyroid mass (甲状腺腫瘤)					
< 65 years	0	0	0	1 (2.1%)	1 (0.5%)
>= 65 years	0	0	0	0	0
< 75 years	0	0	0	1 (1.3%)	1 (0.3%)
>= 75 years	0	.	0	.	0

System Organ Class Preferred Term Age	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
Social circumstances (社会環境)					
< 65 years	1 (0.9%)	0	0	0	0
>= 65 years	0	0	0	0	0
< 75 years	1 (0.6%)	0	0	0	0
>= 75 years	0	.	0	.	0
Menopause (閉経)					
< 65 years	1 (0.9%)	0	0	0	0
>= 65 years	0	0	0	0	0
< 75 years	1 (0.6%)	0	0	0	0
>= 75 years	0	.	0	.	0
Surgical and medical procedures (外科および内科処置)					
< 65 years	0	0	0	0	0
>= 65 years	0	0	1 (1.2%)	0	1 (0.8%)
< 75 years	0	0	1 (0.6%)	0	1 (0.3%)
>= 75 years	0	.	0	.	0
Blepharoplasty (眼瞼形成)					
< 65 years	0	0	0	0	0
>= 65 years	0	0	1 (1.2%)	0	1 (0.8%)
< 75 years	0	0	1 (0.6%)	0	1 (0.3%)
>= 75 years	0	.	0	.	0

- Abbreviations: bid, Twice a day; AE, Adverse event; TEAE, Treatment Emergent AE
- All adverse events were coded using MedDRA dictionary version 20.1.
- Percentages are based on "Number of patients".

Control No:<<t-s-162-subae-24wdb.sas, 2020-03-06T00:12:38>>

Table S-163 Subgroup Analysis of Treatment Emergent Adverse Events by Sex, System Organ Class and Preferred Term in 24-Week Double-blind Period with Monotherapy (PXL008-014, PXL008-018; Safety Population)

System Organ Class Preferred Term Sex	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
Number of patients					
Male	127	49	138	54	241
Female	55	26	42	21	89
Any TEAE					
Male	60 (47.2%)	32 (65.3%)	64 (46.4%)	38 (70.4%)	134 (55.6%)
Female	39 (70.9%)	19 (73.1%)	29 (69.0%)	17 (81.0%)	65 (73.0%)
Infections and infestations (感染症および寄生虫症)					
Male	19 (15.0%)	17 (34.7%)	30 (21.7%)	17 (31.5%)	64 (26.6%)
Female	13 (23.6%)	10 (38.5%)	20 (47.6%)	9 (42.9%)	39 (43.8%)
Nasopharyngitis (上咽頭炎)					
Male	11 (8.7%)	13 (26.5%)	20 (14.5%)	11 (20.4%)	44 (18.3%)
Female	9 (16.4%)	7 (26.9%)	13 (31.0%)	7 (33.3%)	27 (30.3%)
Bronchitis (気管支炎)					
Male	1 (0.8%)	1 (2.0%)	1 (0.7%)	1 (1.9%)	3 (1.2%)
Female	0	2 (7.7%)	1 (2.4%)	0	3 (3.4%)
Gastroenteritis (胃腸炎)					
Male	2 (1.6%)	1 (2.0%)	0	0	1 (0.4%)
Female	0	1 (3.8%)	2 (4.8%)	0	3 (3.4%)
Pharyngitis (咽頭炎)					
Male	1 (0.8%)	0	1 (0.7%)	0	1 (0.4%)
Female	1 (1.8%)	1 (3.8%)	2 (4.8%)	0	3 (3.4%)
Periodontitis (歯周炎)					
Male	2 (1.6%)	0	1 (0.7%)	0	1 (0.4%)
Female	0	1 (3.8%)	0	1 (4.8%)	2 (2.2%)
Influenza (インフルエンザ)					
Male	0	0	3 (2.2%)	1 (1.9%)	4 (1.7%)
Female	0	0	0	0	0
Upper respiratory tract infection (上気道感染)					
Male	1 (0.8%)	0	0	1 (1.9%)	1 (0.4%)
Female	1 (1.8%)	0	1 (2.4%)	0	1 (1.1%)
Conjunctivitis (結膜炎)					
Male	0	0	3 (2.2%)	0	3 (1.2%)
Female	0	0	0	0	0
Cystitis (膀胱炎)					
Male	0	1 (2.0%)	0	0	1 (0.4%)
Female	1 (1.8%)	1 (3.8%)	0	0	1 (1.1%)
Otitis externa (外耳炎)					
Male	1 (0.8%)	0	0	1 (1.9%)	1 (0.4%)
Female	0	0	1 (2.4%)	0	1 (1.1%)

System Organ Class Preferred Term Sex	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
Gastroenteritis viral (ウイルス性胃腸炎)					
Male	0	0	0	0	0
Female	1 (1.8%)	0	0	1 (4.8%)	1 (1.1%)
Herpes zoster (帯状疱疹)					
Male	0	0	0	1 (1.9%)	1 (0.4%)
Female	1 (1.8%)	0	0	0	0
Infected dermal cyst (感染性皮膚嚢腫)					
Male	0	0	1 (0.7%)	0	1 (0.4%)
Female	1 (1.8%)	0	0	0	0
Oral herpes (口腔ヘルペス)					
Male	1 (0.8%)	0	0	0	0
Female	1 (1.8%)	0	0	0	0
Asymptomatic bacteriuria (無症候性細菌尿)					
Male	0	0	1 (0.7%)	0	1 (0.4%)
Female	0	0	0	0	0
Bronchitis bacterial (細菌性気管支炎)					
Male	0	0	1 (0.7%)	0	1 (0.4%)
Female	0	0	0	0	0
Conjunctivitis bacterial (細菌性結膜炎)					
Male	0	0	0	0	0
Female	0	0	0	1 (4.8%)	1 (1.1%)
Gingivitis (歯肉炎)					
Male	1 (0.8%)	0	0	0	0
Female	0	0	0	0	0
Helicobacter infection (ヘリコバクター感染)					
Male	1 (0.8%)	0	0	0	0
Female	0	0	0	0	0
Hordeolum (麦粒腫)					
Male	0	0	1 (0.7%)	0	1 (0.4%)
Female	0	0	0	0	0
Parotitis (耳下腺炎)					
Male	0	0	0	1 (1.9%)	1 (0.4%)
Female	0	0	0	0	0
Pericoronitis (歯冠周囲炎)					
Male	0	0	0	1 (1.9%)	1 (0.4%)
Female	0	0	0	0	0
Pharyngitis streptococcal (レンサ球菌性咽頭炎)					
Male	0	0	0	0	0
Female	1 (1.8%)	0	0	0	0

System Organ Class Preferred Term Sex	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
Pulpitis dental (歯髄炎)					
Male	0	1 (2.0%)	0	0	1 (0.4%)
Female	0	0	0	0	0
Tooth abscess (歯膿瘍)					
Male	0	0	0	0	0
Female	1 (1.8%)	0	0	0	0
Gastrointestinal disorders (胃腸障害)					
Male	9 (7.1%)	8 (16.3%)	16 (11.6%)	13 (24.1%)	37 (15.4%)
Female	11 (20.0%)	3 (11.5%)	10 (23.8%)	11 (52.4%)	24 (27.0%)
Diarrhoea (下痢)					
Male	1 (0.8%)	2 (4.1%)	2 (1.4%)	3 (5.6%)	7 (2.9%)
Female	0	1 (3.8%)	3 (7.1%)	3 (14.3%)	7 (7.9%)
Abdominal discomfort (腹部不快感)					
Male	0	1 (2.0%)	1 (0.7%)	5 (9.3%)	7 (2.9%)
Female	0	0	2 (4.8%)	2 (9.5%)	4 (4.5%)
Vomiting (嘔吐)					
Male	1 (0.8%)	0	0	2 (3.7%)	2 (0.8%)
Female	3 (5.5%)	0	1 (2.4%)	2 (9.5%)	3 (3.4%)
Nausea (悪心)					
Male	0	0	1 (0.7%)	2 (3.7%)	3 (1.2%)
Female	1 (1.8%)	1 (3.8%)	0	3 (14.3%)	4 (4.5%)
Dental caries (齲歯)					
Male	2 (1.6%)	0	1 (0.7%)	0	1 (0.4%)
Female	2 (3.6%)	0	1 (2.4%)	1 (4.8%)	2 (2.2%)
Constipation (便秘)					
Male	0	1 (2.0%)	2 (1.4%)	1 (1.9%)	4 (1.7%)
Female	2 (3.6%)	0	0	0	0
Abdominal pain upper (上腹部痛)					
Male	0	0	0	0	0
Female	1 (1.8%)	2 (7.7%)	1 (2.4%)	0	3 (3.4%)
Gastrooesophageal reflux disease (胃食道逆流性疾患)					
Male	1 (0.8%)	1 (2.0%)	1 (0.7%)	1 (1.9%)	3 (1.2%)
Female	0	0	0	0	0
Dyspepsia (消化不良)					
Male	0	1 (2.0%)	1 (0.7%)	1 (1.9%)	3 (1.2%)
Female	0	0	0	0	0
Gastritis (胃炎)					
Male	0	1 (2.0%)	2 (1.4%)	0	3 (1.2%)
Female	0	0	0	0	0
Periodontal disease (歯周病)					
Male	1 (0.8%)	1 (2.0%)	0	0	1 (0.4%)
Female	0	0	1 (2.4%)	0	1 (1.1%)

System Organ Class Preferred Term Sex	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
Abdominal distension (腹部膨満)					
Male	0	0	1 (0.7%)	1 (1.9%)	2 (0.8%)
Female	0	0	0	0	0
Abdominal pain (腹痛)					
Male	0	0	0	0	0
Female	0	0	2 (4.8%)	0	2 (2.2%)
Chronic gastritis (慢性胃炎)					
Male	0	0	1 (0.7%)	0	1 (0.4%)
Female	0	0	1 (2.4%)	0	1 (1.1%)
Duodenal ulcer (十二指腸潰瘍)					
Male	2 (1.6%)	0	0	0	0
Female	0	0	0	0	0
Faeces soft (軟便)					
Male	1 (0.8%)	0	0	0	0
Female	1 (1.8%)	0	0	0	0
Stomatitis (口内炎)					
Male	0	0	1 (0.7%)	0	1 (0.4%)
Female	0	0	0	1 (4.8%)	1 (1.1%)
Abdominal pain lower (下腹部痛)					
Male	0	0	0	0	0
Female	1 (1.8%)	0	0	0	0
Abnormal faeces (異常便)					
Male	0	0	0	0	0
Female	0	0	1 (2.4%)	0	1 (1.1%)
Duodenal polyp (十二指腸ポリープ)					
Male	0	1 (2.0%)	0	0	1 (0.4%)
Female	0	0	0	0	0
Duodenitis (十二指腸炎)					
Male	0	1 (2.0%)	0	0	1 (0.4%)
Female	0	0	0	0	0
Enteritis (小腸炎)					
Male	0	0	0	0	0
Female	0	0	0	1 (4.8%)	1 (1.1%)
Enterocolitis (腸炎)					
Male	0	0	0	0	0
Female	1 (1.8%)	0	0	0	0
Epigastric discomfort (心窩部不快感)					
Male	0	0	1 (0.7%)	0	1 (0.4%)
Female	0	0	0	0	0
Gastric polyps (胃ポリープ)					
Male	1 (0.8%)	0	0	0	0
Female	0	0	0	0	0
Ileus (イレウス)					
Male	0	0	1 (0.7%)	0	1 (0.4%)

System Organ Class Preferred Term Sex	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
Female	0	0	0	0	0
Large intestine polyp (大腸ポリープ)					
Male	0	0	1 (0.7%)	0	1 (0.4%)
Female	0	0	0	0	0
Loose tooth (弛緩歯)					
Male	0	0	0	0	0
Female	0	0	1 (2.4%)	0	1 (1.1%)
Melaena (メレナ)					
Male	1 (0.8%)	0	0	0	0
Female	0	0	0	0	0
Tooth loss (歯の脱落)					
Male	0	0	0	0	0
Female	1 (1.8%)	0	0	0	0
Metabolism and nutrition disorders (代謝および栄養障害)					
Male	15 (11.8%)	6 (12.2%)	8 (5.8%)	4 (7.4%)	18 (7.5%)
Female	6 (10.9%)	2 (7.7%)	1 (2.4%)	1 (4.8%)	4 (4.5%)
Hyperglycaemia (高血糖)					
Male	10 (7.9%)	2 (4.1%)	1 (0.7%)	0	3 (1.2%)
Female	6 (10.9%)	1 (3.8%)	0	1 (4.8%)	2 (2.2%)
Hypoglycaemia (低血糖)					
Male	2 (1.6%)	4 (8.2%)	5 (3.6%)	4 (7.4%)	13 (5.4%)
Female	0	1 (3.8%)	0	0	1 (1.1%)
Dyslipidaemia (脂質異常症)					
Male	3 (2.4%)	0	1 (0.7%)	0	1 (0.4%)
Female	0	0	1 (2.4%)	0	1 (1.1%)
Hyperuricaemia (高尿酸血症)					
Male	1 (0.8%)	0	1 (0.7%)	0	1 (0.4%)
Female	0	0	0	0	0
Musculoskeletal and connective tissue disorders (筋骨格系および結合組織障害)					
Male	9 (7.1%)	5 (10.2%)	10 (7.2%)	3 (5.6%)	18 (7.5%)
Female	8 (14.5%)	4 (15.4%)	1 (2.4%)	2 (9.5%)	7 (7.9%)
Arthralgia (関節痛)					
Male	3 (2.4%)	0	1 (0.7%)	1 (1.9%)	2 (0.8%)
Female	1 (1.8%)	1 (3.8%)	0	0	1 (1.1%)
Back pain (背部痛)					
Male	0	2 (4.1%)	1 (0.7%)	1 (1.9%)	4 (1.7%)
Female	0	2 (7.7%)	0	0	2 (2.2%)
Muscle spasms (筋痙縮)					
Male	1 (0.8%)	0	3 (2.2%)	0	3 (1.2%)

System Organ Class Preferred Term Sex	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
Female	2 (3.6%)	0	0	0	0
Periarthritis (関節周囲炎)					
Male	2 (1.6%)	0	1 (0.7%)	0	1 (0.4%)
Female	0	0	0	0	0
Musculoskeletal pain (筋骨格痛)					
Male	0	0	0	1 (1.9%)	1 (0.4%)
Female	1 (1.8%)	0	0	0	0
Musculoskeletal stiffness (筋骨格硬直)					
Male	1 (0.8%)	0	0	0	0
Female	0	1 (3.8%)	0	0	1 (1.1%)
Osteoarthritis (変形性関節症)					
Male	1 (0.8%)	0	0	0	0
Female	0	0	1 (2.4%)	0	1 (1.1%)
Plantar fasciitis (足底筋膜炎)					
Male	1 (0.8%)	0	0	0	0
Female	1 (1.8%)	0	0	0	0
Arthritis (関節炎)					
Male	0	1 (2.0%)	0	0	1 (0.4%)
Female	0	0	0	0	0
Fasciitis (筋膜炎)					
Male	0	0	0	0	0
Female	1 (1.8%)	0	0	0	0
Intervertebral disc degeneration (椎間板変性症)					
Male	0	0	1 (0.7%)	0	1 (0.4%)
Female	0	0	0	0	0
Intervertebral disc protrusion (椎間板突出)					
Male	0	0	0	0	0
Female	0	1 (3.8%)	0	0	1 (1.1%)
Joint swelling (関節腫脹)					
Male	0	0	0	0	0
Female	1 (1.8%)	0	0	0	0
Mastication disorder (咀嚼障害)					
Male	0	0	0	0	0
Female	0	0	0	1 (4.8%)	1 (1.1%)
Muscular weakness (筋力低下)					
Male	0	0	1 (0.7%)	0	1 (0.4%)
Female	0	0	0	0	0
Musculoskeletal chest pain (筋骨格系胸痛)					
Male	0	1 (2.0%)	0	0	1 (0.4%)
Female	0	0	0	0	0
Myalgia (筋肉痛)					

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Male	0	0	1 (0.7%)	0	1 (0.4%)
Female	0	0	0	0	0
Neck pain (頚部痛)					
Male	0	0	0	0	0
Female	0	0	0	1 (4.8%)	1 (1.1%)
Osteoporosis (骨粗鬆症)					
Male	0	0	0	0	0
Female	1 (1.8%)	0	0	0	0
Pain in extremity (四肢痛)					
Male	0	1 (2.0%)	0	0	1 (0.4%)
Female	0	0	0	0	0
Spinal osteoarthritis (変形性脊椎症)					
Male	0	0	1 (0.7%)	0	1 (0.4%)
Female	0	0	0	0	0
Spondylolisthesis (脊椎すべり症)					
Male	1 (0.8%)	0	0	0	0
Female	0	0	0	0	0
Temporomandibular joint syndrome (顎関節症候群)					
Male	0	0	0	0	0
Female	0	0	0	1 (4.8%)	1 (1.1%)
Injury, poisoning and procedural complications (傷害、中毒および処置合併症)					
Male	4 (3.1%)	3 (6.1%)	5 (3.6%)	5 (9.3%)	13 (5.4%)
Female	2 (3.6%)	2 (7.7%)	3 (7.1%)	1 (4.8%)	6 (6.7%)
Contusion (挫傷)					
Male	1 (0.8%)	1 (2.0%)	1 (0.7%)	0	2 (0.8%)
Female	0	1 (3.8%)	0	1 (4.8%)	2 (2.2%)
Arthropod sting (節足動物刺傷)					
Male	0	2 (4.1%)	0	2 (3.7%)	4 (1.7%)
Female	0	0	0	0	0
Hand fracture (手骨折)					
Male	0	0	0	0	0
Female	0	1 (3.8%)	0	1 (4.8%)	2 (2.2%)
Ligament sprain (靱帯捻挫)					
Male	0	0	1 (0.7%)	1 (1.9%)	2 (0.8%)
Female	0	0	0	0	0
Radius fracture (橈骨骨折)					
Male	0	0	0	1 (1.9%)	1 (0.4%)
Female	0	0	1 (2.4%)	0	1 (1.1%)
Skin abrasion (皮膚擦過傷)					
Male	0	0	2 (1.4%)	0	2 (0.8%)

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Female	0	0	0	0	0
Arthropod bite (節足動物咬傷)					
Male	1 (0.8%)	0	0	0	0
Female	0	0	0	0	0
Bone contusion (骨挫傷)					
Male	0	0	0	1 (1.9%)	1 (0.4%)
Female	0	0	0	0	0
Clavicle fracture (鎖骨骨折)					
Male	0	0	0	0	0
Female	0	0	1 (2.4%)	0	1 (1.1%)
Fall (転倒)					
Male	0	0	0	0	0
Female	0	0	0	1 (4.8%)	1 (1.1%)
Femur fracture (大腿骨骨折)					
Male	0	0	0	0	0
Female	0	0	1 (2.4%)	0	1 (1.1%)
Limb injury (四肢損傷)					
Male	1 (0.8%)	0	0	0	0
Female	0	0	0	0	0
Lower limb fracture (下肢骨折)					
Male	0	0	0	0	0
Female	1 (1.8%)	0	0	0	0
Meniscus injury (半月板損傷)					
Male	1 (0.8%)	0	0	0	0
Female	0	0	0	0	0
Muscle rupture (筋断裂)					
Male	0	0	0	0	0
Female	1 (1.8%)	0	0	0	0
Post procedural haemorrhage (処置後出血)					
Male	0	0	0	0	0
Female	0	0	1 (2.4%)	0	1 (1.1%)
Rib fracture (肋骨骨折)					
Male	0	0	0	0	0
Female	0	1 (3.8%)	0	0	1 (1.1%)
Thermal burn (熱傷)					
Male	0	0	1 (0.7%)	0	1 (0.4%)
Female	0	0	0	0	0
Skin and subcutaneous tissue disorders (皮膚および皮下組織障害)					
Male	7 (5.5%)	2 (4.1%)	3 (2.2%)	4 (7.4%)	9 (3.7%)
Female	5 (9.1%)	1 (3.8%)	2 (4.8%)	1 (4.8%)	4 (4.5%)
Eczema (湿疹)					

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Male	1 (0.8%)	1 (2.0%)	1 (0.7%)	3 (5.6%)	5 (2.1%)
Female	1 (1.8%)	1 (3.8%)	1 (2.4%)	0	2 (2.2%)
Dermatitis contact (接触皮膚炎)					
Male	0	0	1 (0.7%)	0	1 (0.4%)
Female	1 (1.8%)	0	0	0	0
Dyshidrotic eczema (異汗性湿疹)					
Male	0	0	1 (0.7%)	0	1 (0.4%)
Female	1 (1.8%)	0	0	0	0
Ingrowing nail (嵌入爪)					
Male	0	0	0	1 (1.9%)	1 (0.4%)
Female	1 (1.8%)	0	0	0	0
Miliaria (汗疹)					
Male	1 (0.8%)	1 (2.0%)	0	0	1 (0.4%)
Female	0	0	0	0	0
Alopecia areata (円形脱毛症)					
Male	1 (0.8%)	0	0	0	0
Female	0	0	0	0	0
Drug eruption (薬疹)					
Male	1 (0.8%)	0	0	0	0
Female	0	0	0	0	0
Dry skin (皮膚乾燥)					
Male	0	0	0	0	0
Female	0	0	1 (2.4%)	0	1 (1.1%)
Eczema asteatotic (皮脂欠乏性湿疹)					
Male	1 (0.8%)	0	0	0	0
Female	0	0	0	0	0
Pruritus (そう痒症)					
Male	1 (0.8%)	0	0	0	0
Female	0	0	0	0	0
Pustular psoriasis (膿疱性乾癬)					
Male	1 (0.8%)	0	0	0	0
Female	0	0	0	0	0
Rash (発疹)					
Male	1 (0.8%)	0	0	0	0
Female	0	0	0	0	0
Toxic skin eruption (中毒性皮疹)					
Male	1 (0.8%)	0	0	0	0
Female	0	0	0	0	0
Urticaria (蕁麻疹)					
Male	0	0	0	0	0
Female	1 (1.8%)	0	0	0	0
Xanthoma (黄色腫)					
Male	0	0	0	0	0
Female	0	0	0	1 (4.8%)	1 (1.1%)

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Nervous system disorders (神経系障害)					
Male	3 (2.4%)	4 (8.2%)	4 (2.9%)	1 (1.9%)	9 (3.7%)
Female	7 (12.7%)	2 (7.7%)	3 (7.1%)	0	5 (5.6%)
Dizziness (浮動性めまい)					
Male	0	0	0	0	0
Female	4 (7.3%)	1 (3.8%)	1 (2.4%)	0	2 (2.2%)
Headache (頭痛)					
Male	0	1 (2.0%)	0	0	1 (0.4%)
Female	2 (3.6%)	1 (3.8%)	1 (2.4%)	0	2 (2.2%)
Cervical radiculopathy (頚髄神経根障害)					
Male	0	0	1 (0.7%)	0	1 (0.4%)
Female	1 (1.8%)	0	0	0	0
Dizziness postural (体位性めまい)					
Male	1 (0.8%)	1 (2.0%)	0	0	1 (0.4%)
Female	0	0	0	0	0
Presyncope (失神寸前の状態)					
Male	0	0	1 (0.7%)	0	1 (0.4%)
Female	0	0	1 (2.4%)	0	1 (1.1%)
Carpal tunnel syndrome (手根管症候群)					
Male	0	0	1 (0.7%)	0	1 (0.4%)
Female	0	0	0	0	0
Dysgeusia (味覚異常)					
Male	0	0	0	1 (1.9%)	1 (0.4%)
Female	0	0	0	0	0
Hypoaesthesia (感覚鈍麻)					
Male	1 (0.8%)	0	0	0	0
Female	0	0	0	0	0
IVth nerve disorder (第 4 脳神経障害)					
Male	0	1 (2.0%)	0	0	1 (0.4%)
Female	0	0	0	0	0
Intercostal neuralgia (肋間神経痛)					
Male	1 (0.8%)	0	0	0	0
Female	0	0	0	0	0
Loss of consciousness (意識消失)					
Male	0	0	0	0	0
Female	0	0	1 (2.4%)	0	1 (1.1%)
Orthostatic intolerance (起立不耐性)					
Male	0	1 (2.0%)	0	0	1 (0.4%)
Female	0	0	0	0	0
Spondylitic myelopathy (脊椎炎性脊髄症)					

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Male	0	0	1 (0.7%)	0	1 (0.4%)
Female	0	0	0	0	0
Thoracic outlet syndrome (胸郭出口症候群)					
Male	0	1 (2.0%)	0	0	1 (0.4%)
Female	0	0	0	0	0
Investigations (臨床検査)					
Male	5 (3.9%)	4 (8.2%)	3 (2.2%)	4 (7.4%)	11 (4.6%)
Female	2 (3.6%)	1 (3.8%)	1 (2.4%)	2 (9.5%)	4 (4.5%)
Culture urine positive (尿培養陽性)					
Male	1 (0.8%)	1 (2.0%)	0	3 (5.6%)	4 (1.7%)
Female	0	0	0	1 (4.8%)	1 (1.1%)
Blood bilirubin increased (血中ビリルビン増加)					
Male	2 (1.6%)	0	0	0	0
Female	0	0	0	0	0
Blood creatine phosphokinase increased (血中クレアチンホスホキナーゼ増加)					
Male	1 (0.8%)	0	0	0	0
Female	1 (1.8%)	0	0	0	0
Gamma-glutamyltransferase increased (γ－グルタミルトランスフェラーゼ増加)					
Male	1 (0.8%)	0	0	0	0
Female	0	0	0	1 (4.8%)	1 (1.1%)
Urine albumin/creatinine ratio increased (尿中アルブミン／クレアチニン比増加)					
Male	1 (0.8%)	0	1 (0.7%)	0	1 (0.4%)
Female	0	0	0	0	0
Activated partial thromboplastin time prolonged (活性化部分トロンボプラスチン時間延長)					
Male	0	0	0	0	0
Female	0	1 (3.8%)	0	0	1 (1.1%)
Alanine aminotransferase increased (アラニンアミノトランスフェラーゼ増加)					
Male	1 (0.8%)	0	0	0	0
Female	0	0	0	0	0
Aspartate aminotransferase increased (アスパラギン酸アミノトランスフェラーゼ増加)					
Male	1 (0.8%)	0	0	0	0
Female	0	0	0	0	0

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Blood glucagon increased (血中グルカゴン増加)					
Male	0	0	0	1 (1.9%)	1 (0.4%)
Female	0	0	0	0	0
Blood pressure increased (血圧上昇)					
Male	0	0	0	0	0
Female	1 (1.8%)	0	0	0	0
C-reactive protein increased (Ｃ－反応性蛋白増加)					
Male	0	0	1 (0.7%)	0	1 (0.4%)
Female	0	0	0	0	0
Electrocardiogram T wave inversion (心電図Ｔ波逆転)					
Male	0	0	0	1 (1.9%)	1 (0.4%)
Female	0	0	0	0	0
Eosinophil count increased (好酸球数増加)					
Male	0	1 (2.0%)	0	0	1 (0.4%)
Female	0	0	0	0	0
International normalised ratio increased (国際標準比増加)					
Male	0	0	0	0	0
Female	0	1 (3.8%)	0	0	1 (1.1%)
Lipase increased (リパーゼ増加)					
Male	0	1 (2.0%)	0	0	1 (0.4%)
Female	0	0	0	0	0
Liver function test increased (肝機能検査値上昇)					
Male	0	0	1 (0.7%)	0	1 (0.4%)
Female	0	0	0	0	0
Neutrophil count decreased (好中球数減少)					
Male	0	0	0	0	0
Female	0	0	1 (2.4%)	0	1 (1.1%)
Occult blood (便潜血)					
Male	0	1 (2.0%)	0	0	1 (0.4%)
Female	0	0	0	0	0
General disorders and administration site conditions (一般・全身障害および投与部位の状態)					
Male	4 (3.1%)	0	4 (2.9%)	2 (3.7%)	6 (2.5%)
Female	1 (1.8%)	1 (3.8%)	0	3 (14.3%)	4 (4.5%)
Fatigue (疲労)					

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Male	0	0	2 (1.4%)	1 (1.9%)	3 (1.2%)
Female	1 (1.8%)	0	0	1 (4.8%)	1 (1.1%)
Malaise (倦怠感)					
Male	1 (0.8%)	0	1 (0.7%)	1 (1.9%)	2 (0.8%)
Female	0	1 (3.8%)	0	0	1 (1.1%)
Pyrexia (発熱)					
Male	2 (1.6%)	0	0	0	0
Female	0	0	0	0	0
Chest discomfort (胸部不快感)					
Male	0	0	1 (0.7%)	0	1 (0.4%)
Female	0	0	0	0	0
Feeling abnormal (異常感)					
Male	0	0	0	0	0
Female	0	0	0	1 (4.8%)	1 (1.1%)
Oedema peripheral (末梢性浮腫)					
Male	0	0	0	0	0
Female	0	0	0	1 (4.8%)	1 (1.1%)
Thirst (口渇)					
Male	1 (0.8%)	0	0	0	0
Female	0	0	0	0	0
Eye disorders (眼障害)					
Male	3 (2.4%)	1 (2.0%)	4 (2.9%)	1 (1.9%)	6 (2.5%)
Female	1 (1.8%)	1 (3.8%)	0	2 (9.5%)	3 (3.4%)
Cataract (白内障)					
Male	1 (0.8%)	0	0	1 (1.9%)	1 (0.4%)
Female	0	0	0	0	0
Chalazion (霰粒腫)					
Male	0	1 (2.0%)	0	0	1 (0.4%)
Female	0	0	0	1 (4.8%)	1 (1.1%)
Diabetic retinopathy (糖尿病網膜症)					
Male	0	0	2 (1.4%)	0	2 (0.8%)
Female	0	0	0	0	0
Glaucoma (緑内障)					
Male	0	0	2 (1.4%)	0	2 (0.8%)
Female	0	0	0	0	0
Vitreous floaters (硝子体浮遊物)					
Male	2 (1.6%)	0	0	0	0
Female	0	0	0	0	0
Dry eye (眼乾燥)					
Male	0	0	0	0	0
Female	1 (1.8%)	0	0	0	0
Eye inflammation (眼の炎症)					
Male	0	0	0	0	0

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Female	0	0	0	1 (4.8%)	1 (1.1%)
Eye swelling (眼部腫脹)					
Male	0	0	0	0	0
Female	0	1 (3.8%)	0	0	1 (1.1%)
Macular fibrosis (黄斑線維症)					
Male	0	0	1 (0.7%)	0	1 (0.4%)
Female	0	0	0	0	0
Respiratory, thoracic and mediastinal disorders (呼吸器、胸郭および縦隔障害)					
Male	1 (0.8%)	2 (4.1%)	0	2 (3.7%)	4 (1.7%)
Female	3 (5.5%)	1 (3.8%)	0	0	1 (1.1%)
Oropharyngeal pain (口腔咽頭痛)					
Male	0	0	0	2 (3.7%)	2 (0.8%)
Female	1 (1.8%)	0	0	0	0
Upper respiratory tract inflammation (上気道の炎症)					
Male	1 (0.8%)	0	0	0	0
Female	1 (1.8%)	1 (3.8%)	0	0	1 (1.1%)
Rhinitis allergic (アレルギー性鼻炎)					
Male	0	2 (4.1%)	0	0	2 (0.8%)
Female	0	0	0	0	0
Allergic cough (アレルギー性咳嗽)					
Male	0	0	0	0	0
Female	1 (1.8%)	0	0	0	0
Asthma (喘息)					
Male	0	0	0	0	0
Female	1 (1.8%)	0	0	0	0
Cardiac disorders (心臓障害)					
Male	2 (1.6%)	0	1 (0.7%)	3 (5.6%)	4 (1.7%)
Female	0	0	1 (2.4%)	0	1 (1.1%)
Palpitations (動悸)					
Male	2 (1.6%)	0	1 (0.7%)	1 (1.9%)	2 (0.8%)
Female	0	0	0	0	0
Atrial fibrillation (心房細動)					
Male	0	0	0	1 (1.9%)	1 (0.4%)
Female	0	0	0	0	0
Bradycardia (徐脈)					
Male	0	0	0	0	0
Female	0	0	1 (2.4%)	0	1 (1.1%)
Ventricular extrasystoles (心室性期外収縮)					
Male	0	0	0	1 (1.9%)	1 (0.4%)

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Female	0	0	0	0	0
Vascular disorders (血管障害)					
Male	3 (2.4%)	0	0	0	0
Female	0	2 (7.7%)	1 (2.4%)	1 (4.8%)	4 (4.5%)
Hypertension (高血圧)					
Male	2 (1.6%)	0	0	0	0
Female	0	2 (7.7%)	1 (2.4%)	1 (4.8%)	4 (4.5%)
Arteriosclerosis (動脈硬化症)					
Male	1 (0.8%)	0	0	0	0
Female	0	0	0	0	0
Ear and labyrinth disorders (耳および迷路障害)					
Male	1 (0.8%)	0	1 (0.7%)	2 (3.7%)	3 (1.2%)
Female	0	0	1 (2.4%)	1 (4.8%)	2 (2.2%)
Vertigo (回転性めまい)					
Male	0	0	1 (0.7%)	1 (1.9%)	2 (0.8%)
Female	0	0	0	1 (4.8%)	1 (1.1%)
Ear congestion (耳閉)					
Male	0	0	0	1 (1.9%)	1 (0.4%)
Female	0	0	0	0	0
Eustachian tube stenosis (耳管狭窄)					
Male	1 (0.8%)	0	0	0	0
Female	0	0	0	0	0
Vertigo positional (頭位性回転性めまい)					
Male	0	0	0	0	0
Female	0	0	1 (2.4%)	0	1 (1.1%)
Hepatobiliary disorders (肝胆道系障害)					
Male	3 (2.4%)	0	1 (0.7%)	1 (1.9%)	2 (0.8%)
Female	0	0	0	1 (4.8%)	1 (1.1%)
Hepatic steatosis (脂肪肝)					
Male	1 (0.8%)	0	0	0	0
Female	0	0	0	1 (4.8%)	1 (1.1%)
Gallbladder polyp (胆嚢ポリープ)					
Male	1 (0.8%)	0	0	0	0
Female	0	0	0	0	0
Hepatic function abnormal (肝機能異常)					
Male	0	0	1 (0.7%)	0	1 (0.4%)
Female	0	0	0	0	0
Hepatomegaly (肝腫大)					

System Organ Class Preferred Term Sex	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
Male	0	0	0	1 (1.9%)	1 (0.4%)
Female	0	0	0	0	0
Liver injury (肝損傷)					
Male	1 (0.8%)	0	0	0	0
Female	0	0	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps) (良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）)					
Male	0	0	3 (2.2%)	1 (1.9%)	4 (1.7%)
Female	0	0	1 (2.4%)	0	1 (1.1%)
Bladder cancer (膀胱癌)					
Male	0	0	1 (0.7%)	0	1 (0.4%)
Female	0	0	0	0	0
Pancreatic carcinoma metastatic (遠隔転移を伴う膵癌)					
Male	0	0	0	1 (1.9%)	1 (0.4%)
Female	0	0	0	0	0
Prostate cancer (前立腺癌)					
Male	0	0	1 (0.7%)	0	1 (0.4%)
Female	0	0	0	0	0
Seborrhoeic keratosis (脂漏性角化症)					
Male	0	0	1 (0.7%)	0	1 (0.4%)
Female	0	0	0	0	0
Solid pseudopapillary tumour of the pancreas (膵の充実性偽乳頭状腫瘍)					
Male	0	0	0	0	0
Female	0	0	1 (2.4%)	0	1 (1.1%)
Psychiatric disorders (精神障害)					
Male	1 (0.8%)	0	0	1 (1.9%)	1 (0.4%)
Female	0	1 (3.8%)	0	0	1 (1.1%)
Insomnia (不眠症)					
Male	0	0	0	1 (1.9%)	1 (0.4%)
Female	0	1 (3.8%)	0	0	1 (1.1%)
Anxiety (不安)					
Male	1 (0.8%)	0	0	0	0
Female	0	0	0	0	0
Renal and urinary disorders (腎および尿路障害)					
Male	1 (0.8%)	0	1 (0.7%)	0	1 (0.4%)
Female	0	1 (3.8%)	0	0	1 (1.1%)
Calculus urinary (尿路結石)					

System Organ Class Preferred Term Sex	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
Male	1 (0.8%)	0	0	0	0
Female	0	0	0	0	0
Diabetic nephropathy (糖尿病性腎症)					
Male	0	0	0	0	0
Female	0	1 (3.8%)	0	0	1 (1.1%)
Ureterolithiasis (尿管結石症)					
Male	0	0	1 (0.7%)	0	1 (0.4%)
Female	0	0	0	0	0
Reproductive system and breast disorders (生殖系および乳房障害)					
Male	1 (0.8%)	0	0	0	0
Female	1 (1.8%)	1 (3.8%)	0	0	1 (1.1%)
Benign prostatic hyperplasia (良性前立腺肥大症)					
Male	1 (0.8%)	0	0	0	0
Female	0	0	0	0	0
Dysmenorrhoea (月経困難症)					
Male	0	0	0	0	0
Female	1 (1.8%)	0	0	0	0
Metrorrhagia (不正子宮出血)					
Male	0	0	0	0	0
Female	0	1 (3.8%)	0	0	1 (1.1%)
Prostatitis (前立腺炎)					
Male	1 (0.8%)	0	0	0	0
Female	0	0	0	0	0
Blood and lymphatic system disorders (血液およびリンパ系障害)					
Male	0	0	1 (0.7%)	0	1 (0.4%)
Female	0	0	0	0	0
Anaemia (貧血)					
Male	0	0	1 (0.7%)	0	1 (0.4%)
Female	0	0	0	0	0
Endocrine disorders (内分泌障害)					
Male	0	0	0	0	0
Female	0	0	0	1 (4.8%)	1 (1.1%)
Thyroid cyst (甲状腺嚢腫)					
Male	0	0	0	0	0
Female	0	0	0	1 (4.8%)	1 (1.1%)
Thyroid mass (甲状腺腫瘤)					
Male	0	0	0	0	0
Female	0	0	0	1 (4.8%)	1 (1.1%)

System Organ Class Preferred Term Sex	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
Social circumstances (社会環境)					
Male	0	0	0	0	0
Female	1 (1.8%)	0	0	0	0
Menopause (閉経)					
Male	0	0	0	0	0
Female	1 (1.8%)	0	0	0	0
Surgical and medical procedures (外科および内科処置)					
Male	0	0	1 (0.7%)	0	1 (0.4%)
Female	0	0	0	0	0
Blepharoplasty (眼瞼形成)					
Male	0	0	1 (0.7%)	0	1 (0.4%)
Female	0	0	0	0	0

- Abbreviations: bid, Twice a day; AE, Adverse event; TEAE, Treatment Emergent AE
- All adverse events were coded using MedDRA dictionary version 20.1.
- Percentages are based on "Number of patients".

Control No:<<t-s-163-subae-24wdb.sas, 2020-03-06T00:12:39>>

Table S-164 Subgroup Analysis of Treatment Emergent Adverse Events by Renal Function, System Organ Class and Preferred Term in 24-Week Double-blind Period with Monotherapy (PXL008-014, PXL008-018; Safety Population)

System Organ Class Preferred Term Renal function	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
Number of patients					
CKD Stage 1	16	9	21	14	44
CKD Stage 2	137	56	131	52	239
CKD Stage 3a	29	10	28	9	47
Any TEAE					
CKD Stage 1	11 (68.8%)	5 (55.6%)	10 (47.6%)	12 (85.7%)	27 (61.4%)
CKD Stage 2	71 (51.8%)	39 (69.6%)	68 (51.9%)	36 (69.2%)	143 (59.8%)
CKD Stage 3a	17 (58.6%)	7 (70.0%)	15 (53.6%)	7 (77.8%)	29 (61.7%)
Infections and infestations (感染症および寄生虫症)					
CKD Stage 1	2 (12.5%)	4 (44.4%)	7 (33.3%)	6 (42.9%)	17 (38.6%)
CKD Stage 2	20 (14.6%)	19 (33.9%)	34 (26.0%)	16 (30.8%)	69 (28.9%)
CKD Stage 3a	10 (34.5%)	4 (40.0%)	9 (32.1%)	4 (44.4%)	17 (36.2%)
Nasopharyngitis (上咽頭炎)					
CKD Stage 1	1 (6.3%)	2 (22.2%)	5 (23.8%)	5 (35.7%)	12 (27.3%)
CKD Stage 2	14 (10.2%)	15 (26.8%)	21 (16.0%)	9 (17.3%)	45 (18.8%)
CKD Stage 3a	5 (17.2%)	3 (30.0%)	7 (25.0%)	4 (44.4%)	14 (29.8%)
Bronchitis (気管支炎)					
CKD Stage 1	0	1 (11.1%)	0	0	1 (2.3%)
CKD Stage 2	1 (0.7%)	2 (3.6%)	1 (0.8%)	1 (1.9%)	4 (1.7%)
CKD Stage 3a	0	0	1 (3.6%)	0	1 (2.1%)
Gastroenteritis (胃腸炎)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	2 (1.5%)	2 (3.6%)	1 (0.8%)	0	3 (1.3%)
CKD Stage 3a	0	0	1 (3.6%)	0	1 (2.1%)
Pharyngitis (咽頭炎)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	1 (0.7%)	1 (1.8%)	3 (2.3%)	0	4 (1.7%)
CKD Stage 3a	1 (3.4%)	0	0	0	0
Periodontitis (歯周炎)					
CKD Stage 1	1 (6.3%)	0	0	0	0
CKD Stage 2	0	0	1 (0.8%)	1 (1.9%)	2 (0.8%)
CKD Stage 3a	1 (3.4%)	1 (10.0%)	0	0	1 (2.1%)
Influenza (インフルエンザ)					
CKD Stage 1	0	0	0	1 (7.1%)	1 (2.3%)
CKD Stage 2	0	0	3 (2.3%)	0	3 (1.3%)
CKD Stage 3a	0	0	0	0	0
Upper respiratory tract infection (上気道感染)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	1 (0.7%)	0	1 (0.8%)	1 (1.9%)	2 (0.8%)
CKD Stage 3a	1 (3.4%)	0	0	0	0

System Organ Class Preferred Term Renal function	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
Conjunctivitis (結膜炎)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	0	3 (2.3%)	0	3 (1.3%)
CKD Stage 3a	0	0	0	0	0
Cystitis (膀胱炎)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	1 (0.7%)	1 (1.8%)	0	0	1 (0.4%)
CKD Stage 3a	0	1 (10.0%)	0	0	1 (2.1%)
Otitis externa (外耳炎)					
CKD Stage 1	0	0	1 (4.8%)	0	1 (2.3%)
CKD Stage 2	1 (0.7%)	0	0	1 (1.9%)	1 (0.4%)
CKD Stage 3a	0	0	0	0	0
Gastroenteritis viral (ウイルス性胃腸炎)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	1 (0.7%)	0	0	1 (1.9%)	1 (0.4%)
CKD Stage 3a	0	0	0	0	0
Herpes zoster (帯状疱疹)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	0	0	1 (1.9%)	1 (0.4%)
CKD Stage 3a	1 (3.4%)	0	0	0	0
Infected dermal cyst (感染性皮膚嚢腫)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	1 (0.7%)	0	0	0	0
CKD Stage 3a	0	0	1 (3.6%)	0	1 (2.1%)
Oral herpes (口腔ヘルペス)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	2 (1.5%)	0	0	0	0
CKD Stage 3a	0	0	0	0	0
Asymptomatic bacteriuria (無症候性細菌尿)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	0	1 (0.8%)	0	1 (0.4%)
CKD Stage 3a	0	0	0	0	0
Bronchitis bacterial (細菌性気管支炎)					
CKD Stage 1	0	0	1 (4.8%)	0	1 (2.3%)
CKD Stage 2	0	0	0	0	0
CKD Stage 3a	0	0	0	0	0
Conjunctivitis bacterial (細菌性結膜炎)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	0	0	1 (1.9%)	1 (0.4%)
CKD Stage 3a	0	0	0	0	0
Gingivitis (歯肉炎)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	1 (0.7%)	0	0	0	0

System Organ Class Preferred Term Renal function	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
CKD Stage 3a	0	0	0	0	0
Helicobacter infection (ヘリコバクター感染)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	0	0	0	0
CKD Stage 3a	1 (3.4%)	0	0	0	0
Hordeolum (麦粒腫)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	0	1 (0.8%)	0	1 (0.4%)
CKD Stage 3a	0	0	0	0	0
Parotitis (耳下腺炎)					
CKD Stage 1	0	0	0	1 (7.1%)	1 (2.3%)
CKD Stage 2	0	0	0	0	0
CKD Stage 3a	0	0	0	0	0
Pericoronitis (歯冠周囲炎)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	0	0	1 (1.9%)	1 (0.4%)
CKD Stage 3a	0	0	0	0	0
Pharyngitis streptococcal (レンサ球菌性咽頭炎)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	1 (0.7%)	0	0	0	0
CKD Stage 3a	0	0	0	0	0
Pulpitis dental (歯髄炎)					
CKD Stage 1	0	1 (11.1%)	0	0	1 (2.3%)
CKD Stage 2	0	0	0	0	0
CKD Stage 3a	0	0	0	0	0
Tooth abscess (歯膿瘍)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	1 (0.7%)	0	0	0	0
CKD Stage 3a	0	0	0	0	0
Gastrointestinal disorders (胃腸障害)					
CKD Stage 1	6 (37.5%)	0	4 (19.0%)	3 (21.4%)	7 (15.9%)
CKD Stage 2	11 (8.0%)	9 (16.1%)	19 (14.5%)	17 (32.7%)	45 (18.8%)
CKD Stage 3a	3 (10.3%)	2 (20.0%)	3 (10.7%)	4 (44.4%)	9 (19.1%)
Diarrhoea (下痢)					
CKD Stage 1	1 (6.3%)	0	0	1 (7.1%)	1 (2.3%)
CKD Stage 2	0	2 (3.6%)	5 (3.8%)	4 (7.7%)	11 (4.6%)
CKD Stage 3a	0	1 (10.0%)	0	1 (11.1%)	2 (4.3%)
Abdominal discomfort (腹部不快感)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	1 (1.8%)	3 (2.3%)	7 (13.5%)	11 (4.6%)
CKD Stage 3a	0	0	0	0	0
Vomiting (嘔吐)					

System Organ Class Preferred Term Renal function	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
CKD Stage 1	2 (12.5%)	0	0	0	0
CKD Stage 2	1 (0.7%)	0	1 (0.8%)	3 (5.8%)	4 (1.7%)
CKD Stage 3a	1 (3.4%)	0	0	1 (11.1%)	1 (2.1%)
Nausea (悪心)					
CKD Stage 1	0	0	0	1 (7.1%)	1 (2.3%)
CKD Stage 2	1 (0.7%)	1 (1.8%)	1 (0.8%)	3 (5.8%)	5 (2.1%)
CKD Stage 3a	0	0	0	1 (11.1%)	1 (2.1%)
Dental caries (齲歯)					
CKD Stage 1	2 (12.5%)	0	0	0	0
CKD Stage 2	1 (0.7%)	0	2 (1.5%)	1 (1.9%)	3 (1.3%)
CKD Stage 3a	1 (3.4%)	0	0	0	0
Constipation (便秘)					
CKD Stage 1	0	0	1 (4.8%)	0	1 (2.3%)
CKD Stage 2	2 (1.5%)	1 (1.8%)	0	0	1 (0.4%)
CKD Stage 3a	0	0	1 (3.6%)	1 (11.1%)	2 (4.3%)
Abdominal pain upper (上腹部痛)					
CKD Stage 1	1 (6.3%)	0	0	0	0
CKD Stage 2	0	1 (1.8%)	1 (0.8%)	0	2 (0.8%)
CKD Stage 3a	0	1 (10.0%)	0	0	1 (2.1%)
Gastrooesophageal reflux disease (胃食道逆流性疾患)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	1 (0.7%)	1 (1.8%)	1 (0.8%)	1 (1.9%)	3 (1.3%)
CKD Stage 3a	0	0	0	0	0
Dyspepsia (消化不良)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	1 (1.8%)	1 (0.8%)	1 (1.9%)	3 (1.3%)
CKD Stage 3a	0	0	0	0	0
Gastritis (胃炎)					
CKD Stage 1	0	0	1 (4.8%)	0	1 (2.3%)
CKD Stage 2	0	1 (1.8%)	1 (0.8%)	0	2 (0.8%)
CKD Stage 3a	0	0	0	0	0
Periodontal disease (歯周病)					
CKD Stage 1	0	0	1 (4.8%)	0	1 (2.3%)
CKD Stage 2	1 (0.7%)	1 (1.8%)	0	0	1 (0.4%)
CKD Stage 3a	0	0	0	0	0
Abdominal distension (腹部膨満)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	0	1 (0.8%)	1 (1.9%)	2 (0.8%)
CKD Stage 3a	0	0	0	0	0
Abdominal pain (腹痛)					
CKD Stage 1	0	0	1 (4.8%)	0	1 (2.3%)
CKD Stage 2	0	0	1 (0.8%)	0	1 (0.4%)
CKD Stage 3a	0	0	0	0	0
Chronic gastritis (慢性胃炎)					

System Organ Class Preferred Term Renal function	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
CKD Stage 1	0	0	1 (4.8%)	0	1 (2.3%)
CKD Stage 2	0	0	0	0	0
CKD Stage 3a	0	0	1 (3.6%)	0	1 (2.1%)
Duodenal ulcer (十二指腸潰瘍)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	2 (1.5%)	0	0	0	0
CKD Stage 3a	0	0	0	0	0
Faeces soft (軟便)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	2 (1.5%)	0	0	0	0
CKD Stage 3a	0	0	0	0	0
Stomatitis (口内炎)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	0	0	1 (1.9%)	1 (0.4%)
CKD Stage 3a	0	0	1 (3.6%)	0	1 (2.1%)
Abdominal pain lower (下腹部痛)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	0	0	0	0
CKD Stage 3a	1 (3.4%)	0	0	0	0
Abnormal faeces (異常便)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	0	1 (0.8%)	0	1 (0.4%)
CKD Stage 3a	0	0	0	0	0
Duodenal polyp (十二指腸ポリープ)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	1 (1.8%)	0	0	1 (0.4%)
CKD Stage 3a	0	0	0	0	0
Duodenitis (十二指腸炎)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	1 (1.8%)	0	0	1 (0.4%)
CKD Stage 3a	0	0	0	0	0
Enteritis (小腸炎)					
CKD Stage 1	0	0	0	1 (7.1%)	1 (2.3%)
CKD Stage 2	0	0	0	0	0
CKD Stage 3a	0	0	0	0	0
Enterocolitis (腸炎)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	1 (0.7%)	0	0	0	0
CKD Stage 3a	0	0	0	0	0
Epigastric discomfort (心窩部不快感)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	0	1 (0.8%)	0	1 (0.4%)
CKD Stage 3a	0	0	0	0	0
Gastric polyps (胃ポリープ)					
CKD Stage 1	0	0	0	0	0

System Organ Class Preferred Term Renal function	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
CKD Stage 2	1 (0.7%)	0	0	0	0
CKD Stage 3a	0	0	0	0	0
Ileus (イレウス)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	0	1 (0.8%)	0	1 (0.4%)
CKD Stage 3a	0	0	0	0	0
Large intestine polyp (大腸ポリープ)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	0	1 (0.8%)	0	1 (0.4%)
CKD Stage 3a	0	0	0	0	0
Loose tooth (弛緩歯)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	0	1 (0.8%)	0	1 (0.4%)
CKD Stage 3a	0	0	0	0	0
Melaena (メレナ)					
CKD Stage 1	1 (6.3%)	0	0	0	0
CKD Stage 2	0	0	0	0	0
CKD Stage 3a	0	0	0	0	0
Tooth loss (歯の脱落)					
CKD Stage 1	1 (6.3%)	0	0	0	0
CKD Stage 2	0	0	0	0	0
CKD Stage 3a	0	0	0	0	0
Metabolism and nutrition disorders (代謝および栄養障害)					
CKD Stage 1	1 (6.3%)	1 (11.1%)	0	1 (7.1%)	2 (4.5%)
CKD Stage 2	16 (11.7%)	6 (10.7%)	7 (5.3%)	4 (7.7%)	17 (7.1%)
CKD Stage 3a	4 (13.8%)	1 (10.0%)	2 (7.1%)	0	3 (6.4%)
Hyperglycaemia (高血糖)					
CKD Stage 1	1 (6.3%)	0	0	0	0
CKD Stage 2	13 (9.5%)	3 (5.4%)	1 (0.8%)	1 (1.9%)	5 (2.1%)
CKD Stage 3a	2 (6.9%)	0	0	0	0
Hypoglycaemia (低血糖)					
CKD Stage 1	0	1 (11.1%)	0	1 (7.1%)	2 (4.5%)
CKD Stage 2	1 (0.7%)	3 (5.4%)	3 (2.3%)	3 (5.8%)	9 (3.8%)
CKD Stage 3a	1 (3.4%)	1 (10.0%)	2 (7.1%)	0	3 (6.4%)
Dyslipidaemia (脂質異常症)					
CKD Stage 1	1 (6.3%)	0	0	0	0
CKD Stage 2	1 (0.7%)	0	2 (1.5%)	0	2 (0.8%)
CKD Stage 3a	1 (3.4%)	0	0	0	0
Hyperuricaemia (高尿酸血症)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	1 (0.7%)	0	1 (0.8%)	0	1 (0.4%)
CKD Stage 3a	0	0	0	0	0

System Organ Class Preferred Term Renal function	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
Musculoskeletal and connective tissue disorders (筋骨格系および結合組織障害)					
CKD Stage 1	2 (12.5%)	1 (11.1%)	0	0	1 (2.3%)
CKD Stage 2	14 (10.2%)	7 (12.5%)	9 (6.9%)	4 (7.7%)	20 (8.4%)
CKD Stage 3a	1 (3.4%)	1 (10.0%)	2 (7.1%)	1 (11.1%)	4 (8.5%)
Arthralgia (関節痛)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	4 (2.9%)	1 (1.8%)	1 (0.8%)	1 (1.9%)	3 (1.3%)
CKD Stage 3a	0	0	0	0	0
Back pain (背部痛)					
CKD Stage 1	0	1 (11.1%)	0	0	1 (2.3%)
CKD Stage 2	0	3 (5.4%)	1 (0.8%)	0	4 (1.7%)
CKD Stage 3a	0	0	0	1 (11.1%)	1 (2.1%)
Muscle spasms (筋痙縮)					
CKD Stage 1	1 (6.3%)	0	0	0	0
CKD Stage 2	2 (1.5%)	0	3 (2.3%)	0	3 (1.3%)
CKD Stage 3a	0	0	0	0	0
Periarthritis (関節周囲炎)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	2 (1.5%)	0	1 (0.8%)	0	1 (0.4%)
CKD Stage 3a	0	0	0	0	0
Musculoskeletal pain (筋骨格痛)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	1 (0.7%)	0	0	1 (1.9%)	1 (0.4%)
CKD Stage 3a	0	0	0	0	0
Musculoskeletal stiffness (筋骨格硬直)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	1 (0.7%)	1 (1.8%)	0	0	1 (0.4%)
CKD Stage 3a	0	0	0	0	0
Osteoarthritis (変形性関節症)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	1 (0.7%)	0	0	0	0
CKD Stage 3a	0	0	1 (3.6%)	0	1 (2.1%)
Plantar fasciitis (足底筋膜炎)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	2 (1.5%)	0	0	0	0
CKD Stage 3a	0	0	0	0	0
Arthritis (関節炎)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	1 (1.8%)	0	0	1 (0.4%)
CKD Stage 3a	0	0	0	0	0
Fasciitis (筋膜炎)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	0	0	0	0

System Organ Class Preferred Term Renal function	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
CKD Stage 3a	1 (3.4%)	0	0	0	0
Intervertebral disc degeneration (椎間板変性症)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	0	1 (0.8%)	0	1 (0.4%)
CKD Stage 3a	0	0	0	0	0
Intervertebral disc protrusion (椎間板突出)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	1 (1.8%)	0	0	1 (0.4%)
CKD Stage 3a	0	0	0	0	0
Joint swelling (関節腫脹)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	1 (0.7%)	0	0	0	0
CKD Stage 3a	0	0	0	0	0
Mastication disorder (咀嚼障害)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	0	0	1 (1.9%)	1 (0.4%)
CKD Stage 3a	0	0	0	0	0
Muscular weakness (筋力低下)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	0	0	0	0
CKD Stage 3a	0	0	1 (3.6%)	0	1 (2.1%)
Musculoskeletal chest pain (筋骨格系胸痛)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	1 (1.8%)	0	0	1 (0.4%)
CKD Stage 3a	0	0	0	0	0
Myalgia (筋肉痛)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	0	1 (0.8%)	0	1 (0.4%)
CKD Stage 3a	0	0	0	0	0
Neck pain (頚部痛)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	0	0	1 (1.9%)	1 (0.4%)
CKD Stage 3a	0	0	0	0	0
Osteoporosis (骨粗鬆症)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	1 (0.7%)	0	0	0	0
CKD Stage 3a	0	0	0	0	0
Pain in extremity (四肢痛)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	0	0	0	0
CKD Stage 3a	0	1 (10.0%)	0	0	1 (2.1%)
Spinal osteoarthritis (変形性脊椎症)					

System Organ Class Preferred Term Renal function	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	0	1 (0.8%)	0	1 (0.4%)
CKD Stage 3a	0	0	0	0	0
Spondylolisthesis (脊椎すべり症)					
CKD Stage 1	1 (6.3%)	0	0	0	0
CKD Stage 2	0	0	0	0	0
CKD Stage 3a	0	0	0	0	0
Temporomandibular joint syndrome (顎関節症候群)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	0	0	1 (1.9%)	1 (0.4%)
CKD Stage 3a	0	0	0	0	0
Injury, poisoning and procedural complications (傷害、中毒および処置合併症)					
CKD Stage 1	0	1 (11.1%)	1 (4.8%)	2 (14.3%)	4 (9.1%)
CKD Stage 2	5 (3.6%)	3 (5.4%)	6 (4.6%)	4 (7.7%)	13 (5.4%)
CKD Stage 3a	1 (3.4%)	1 (10.0%)	1 (3.6%)	0	2 (4.3%)
Contusion (挫傷)					
CKD Stage 1	0	1 (11.1%)	0	1 (7.1%)	2 (4.5%)
CKD Stage 2	1 (0.7%)	1 (1.8%)	1 (0.8%)	0	2 (0.8%)
CKD Stage 3a	0	0	0	0	0
Arthropod sting (節足動物刺傷)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	1 (1.8%)	0	2 (3.8%)	3 (1.3%)
CKD Stage 3a	0	1 (10.0%)	0	0	1 (2.1%)
Hand fracture (手骨折)					
CKD Stage 1	0	0	0	1 (7.1%)	1 (2.3%)
CKD Stage 2	0	1 (1.8%)	0	0	1 (0.4%)
CKD Stage 3a	0	0	0	0	0
Ligament sprain (靱帯捻挫)					
CKD Stage 1	0	0	1 (4.8%)	1 (7.1%)	2 (4.5%)
CKD Stage 2	0	0	0	0	0
CKD Stage 3a	0	0	0	0	0
Radius fracture (橈骨骨折)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	0	1 (0.8%)	1 (1.9%)	2 (0.8%)
CKD Stage 3a	0	0	0	0	0
Skin abrasion (皮膚擦過傷)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	0	1 (0.8%)	0	1 (0.4%)
CKD Stage 3a	0	0	1 (3.6%)	0	1 (2.1%)
Arthropod bite (節足動物咬傷)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	1 (0.7%)	0	0	0	0

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CKD Stage 3a	0	0	0	0	0
Bone contusion (骨挫傷)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	0	0	1 (1.9%)	1 (0.4%)
CKD Stage 3a	0	0	0	0	0
Clavicle fracture (鎖骨骨折)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	0	1 (0.8%)	0	1 (0.4%)
CKD Stage 3a	0	0	0	0	0
Fall (転倒)					
CKD Stage 1	0	0	0	1 (7.1%)	1 (2.3%)
CKD Stage 2	0	0	0	0	0
CKD Stage 3a	0	0	0	0	0
Femur fracture (大腿骨骨折)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	0	1 (0.8%)	0	1 (0.4%)
CKD Stage 3a	0	0	0	0	0
Limb injury (四肢損傷)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	0	0	0	0
CKD Stage 3a	1 (3.4%)	0	0	0	0
Lower limb fracture (下肢骨折)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	1 (0.7%)	0	0	0	0
CKD Stage 3a	0	0	0	0	0
Meniscus injury (半月板損傷)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	1 (0.7%)	0	0	0	0
CKD Stage 3a	0	0	0	0	0
Muscle rupture (筋断裂)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	1 (0.7%)	0	0	0	0
CKD Stage 3a	0	0	0	0	0
Post procedural haemorrhage (処置後出血)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	0	1 (0.8%)	0	1 (0.4%)
CKD Stage 3a	0	0	0	0	0
Rib fracture (肋骨骨折)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	1 (1.8%)	0	0	1 (0.4%)
CKD Stage 3a	0	0	0	0	0
Thermal burn (熱傷)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	0	1 (0.8%)	0	1 (0.4%)

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CKD Stage 3a	0	0	0	0	0
Skin and subcutaneous tissue disorders (皮膚および皮下組織障害)					
CKD Stage 1	3 (18.8%)	0	1 (4.8%)	1 (7.1%)	2 (4.5%)
CKD Stage 2	8 (5.8%)	3 (5.4%)	4 (3.1%)	3 (5.8%)	10 (4.2%)
CKD Stage 3a	1 (3.4%)	0	0	1 (11.1%)	1 (2.1%)
Eczema (湿疹)					
CKD Stage 1	1 (6.3%)	0	1 (4.8%)	1 (7.1%)	2 (4.5%)
CKD Stage 2	1 (0.7%)	2 (3.6%)	1 (0.8%)	2 (3.8%)	5 (2.1%)
CKD Stage 3a	0	0	0	0	0
Dermatitis contact (接触皮膚炎)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	1 (0.7%)	0	1 (0.8%)	0	1 (0.4%)
CKD Stage 3a	0	0	0	0	0
Dyshidrotic eczema (異汗性湿疹)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	1 (0.7%)	0	1 (0.8%)	0	1 (0.4%)
CKD Stage 3a	0	0	0	0	0
Ingrowing nail (嵌入爪)					
CKD Stage 1	1 (6.3%)	0	0	0	0
CKD Stage 2	0	0	0	1 (1.9%)	1 (0.4%)
CKD Stage 3a	0	0	0	0	0
Miliaria (汗疹)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	1 (0.7%)	1 (1.8%)	0	0	1 (0.4%)
CKD Stage 3a	0	0	0	0	0
Alopecia areata (円形脱毛症)					
CKD Stage 1	1 (6.3%)	0	0	0	0
CKD Stage 2	0	0	0	0	0
CKD Stage 3a	0	0	0	0	0
Drug eruption (薬疹)					
CKD Stage 1	1 (6.3%)	0	0	0	0
CKD Stage 2	0	0	0	0	0
CKD Stage 3a	0	0	0	0	0
Dry skin (皮膚乾燥)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	0	1 (0.8%)	0	1 (0.4%)
CKD Stage 3a	0	0	0	0	0
Eczema asteatotic (皮脂欠乏性湿疹)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	1 (0.7%)	0	0	0	0
CKD Stage 3a	0	0	0	0	0
Pruritus (そう痒症)					
CKD Stage 1	0	0	0	0	0

System Organ Class Preferred Term Renal function	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
CKD Stage 2	1 (0.7%)	0	0	0	0
CKD Stage 3a	0	0	0	0	0
Pustular psoriasis (膿疱性乾癬)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	1 (0.7%)	0	0	0	0
CKD Stage 3a	0	0	0	0	0
Rash (発疹)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	0	0	0	0
CKD Stage 3a	1 (3.4%)	0	0	0	0
Toxic skin eruption (中毒性皮疹)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	1 (0.7%)	0	0	0	0
CKD Stage 3a	0	0	0	0	0
Urticaria (蕁麻疹)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	1 (0.7%)	0	0	0	0
CKD Stage 3a	0	0	0	0	0
Xanthoma (黄色腫)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	0	0	0	0
CKD Stage 3a	0	0	0	1 (11.1%)	1 (2.1%)
Nervous system disorders (神経系障害)					
CKD Stage 1	3 (18.8%)	0	1 (4.8%)	0	1 (2.3%)
CKD Stage 2	6 (4.4%)	6 (10.7%)	5 (3.8%)	1 (1.9%)	12 (5.0%)
CKD Stage 3a	1 (3.4%)	0	1 (3.6%)	0	1 (2.1%)
Dizziness (浮動性めまい)					
CKD Stage 1	1 (6.3%)	0	0	0	0
CKD Stage 2	3 (2.2%)	1 (1.8%)	1 (0.8%)	0	2 (0.8%)
CKD Stage 3a	0	0	0	0	0
Headache (頭痛)					
CKD Stage 1	1 (6.3%)	0	1 (4.8%)	0	1 (2.3%)
CKD Stage 2	1 (0.7%)	2 (3.6%)	0	0	2 (0.8%)
CKD Stage 3a	0	0	0	0	0
Cervical radiculopathy (頚髄神経根障害)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	1 (0.7%)	0	0	0	0
CKD Stage 3a	0	0	1 (3.6%)	0	1 (2.1%)
Dizziness postural (体位性めまい)					
CKD Stage 1	1 (6.3%)	0	0	0	0
CKD Stage 2	0	1 (1.8%)	0	0	1 (0.4%)
CKD Stage 3a	0	0	0	0	0
Presyncope (失神寸前の状態)					

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CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	0	2 (1.5%)	0	2 (0.8%)
CKD Stage 3a	0	0	0	0	0
Carpal tunnel syndrome (手根管症候群)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	0	1 (0.8%)	0	1 (0.4%)
CKD Stage 3a	0	0	0	0	0
Dysgeusia (味覚異常)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	0	0	1 (1.9%)	1 (0.4%)
CKD Stage 3a	0	0	0	0	0
Hypoaesthesia (感覚鈍麻)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	0	0	0	0
CKD Stage 3a	1 (3.4%)	0	0	0	0
IVth nerve disorder (第 4 脳神経障害)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	1 (1.8%)	0	0	1 (0.4%)
CKD Stage 3a	0	0	0	0	0
Intercostal neuralgia (肋間神経痛)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	1 (0.7%)	0	0	0	0
CKD Stage 3a	0	0	0	0	0
Loss of consciousness (意識消失)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	0	1 (0.8%)	0	1 (0.4%)
CKD Stage 3a	0	0	0	0	0
Orthostatic intolerance (起立不耐性)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	1 (1.8%)	0	0	1 (0.4%)
CKD Stage 3a	0	0	0	0	0
Spondylitic myelopathy (脊椎炎性脊髄症)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	0	1 (0.8%)	0	1 (0.4%)
CKD Stage 3a	0	0	0	0	0
Thoracic outlet syndrome (胸郭出口症候群)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	1 (1.8%)	0	0	1 (0.4%)
CKD Stage 3a	0	0	0	0	0
Investigations (臨床検査)					
CKD Stage 1	2 (12.5%)	1 (11.1%)	0	2 (14.3%)	3 (6.8%)

System Organ Class Preferred Term Renal function	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
CKD Stage 2	4 (2.9%)	2 (3.6%)	4 (3.1%)	3 (5.8%)	9 (3.8%)
CKD Stage 3a	1 (3.4%)	2 (20.0%)	0	1 (11.1%)	3 (6.4%)
Culture urine positive (尿培養陽性)					
CKD Stage 1	0	0	0	2 (14.3%)	2 (4.5%)
CKD Stage 2	1 (0.7%)	0	0	1 (1.9%)	1 (0.4%)
CKD Stage 3a	0	1 (10.0%)	0	1 (11.1%)	2 (4.3%)
Blood bilirubin increased (血中ビリルビン増加)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	2 (1.5%)	0	0	0	0
CKD Stage 3a	0	0	0	0	0
Blood creatine phosphokinase increased (血中クレアチンホスホキナーゼ増加)					
CKD Stage 1	1 (6.3%)	0	0	0	0
CKD Stage 2	1 (0.7%)	0	0	0	0
CKD Stage 3a	0	0	0	0	0
Gamma-glutamyltransferase increased (γ－グルタミルトランスフェラーゼ増加)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	1 (0.7%)	0	0	1 (1.9%)	1 (0.4%)
CKD Stage 3a	0	0	0	0	0
Urine albumin/creatinine ratio increased (尿中アルブミン／クレアチニン比増加)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	0	1 (0.8%)	0	1 (0.4%)
CKD Stage 3a	1 (3.4%)	0	0	0	0
Activated partial thromboplastin time prolonged (活性化部分トロンボプラスチン時間延長)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	0	0	0	0
CKD Stage 3a	0	1 (10.0%)	0	0	1 (2.1%)
Alanine aminotransferase increased (アラニンアミノトランスフェラーゼ増加)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	1 (0.7%)	0	0	0	0
CKD Stage 3a	0	0	0	0	0
Aspartate aminotransferase increased (アスパラギン酸アミノトランスフェラーゼ増加)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	1 (0.7%)	0	0	0	0
CKD Stage 3a	0	0	0	0	0

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Blood glucagon increased (血中グルカゴン増加)					
CKD Stage 1	0	0	0	1 (7.1%)	1 (2.3%)
CKD Stage 2	0	0	0	0	0
CKD Stage 3a	0	0	0	0	0
Blood pressure increased (血圧上昇)					
CKD Stage 1	1 (6.3%)	0	0	0	0
CKD Stage 2	0	0	0	0	0
CKD Stage 3a	0	0	0	0	0
C-reactive protein increased (Ｃ－反応性蛋白増加)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	0	1 (0.8%)	0	1 (0.4%)
CKD Stage 3a	0	0	0	0	0
Electrocardiogram T wave inversion (心電図Ｔ波逆転)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	0	0	1 (1.9%)	1 (0.4%)
CKD Stage 3a	0	0	0	0	0
Eosinophil count increased (好酸球数増加)					
CKD Stage 1	0	1 (11.1%)	0	0	1 (2.3%)
CKD Stage 2	0	0	0	0	0
CKD Stage 3a	0	0	0	0	0
International normalised ratio increased (国際標準比増加)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	0	0	0	0
CKD Stage 3a	0	1 (10.0%)	0	0	1 (2.1%)
Lipase increased (リパーゼ増加)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	1 (1.8%)	0	0	1 (0.4%)
CKD Stage 3a	0	0	0	0	0
Liver function test increased (肝機能検査値上昇)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	0	1 (0.8%)	0	1 (0.4%)
CKD Stage 3a	0	0	0	0	0
Neutrophil count decreased (好中球数減少)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	0	1 (0.8%)	0	1 (0.4%)
CKD Stage 3a	0	0	0	0	0
Occult blood (便潜血)					
CKD Stage 1	0	0	0	0	0

System Organ Class Preferred Term Renal function	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
CKD Stage 2	0	1 (1.8%)	0	0	1 (0.4%)
CKD Stage 3a	0	0	0	0	0
General disorders and administration site conditions (一般・全身障害および投与部位の状態)					
CKD Stage 1	1 (6.3%)	0	0	2 (14.3%)	2 (4.5%)
CKD Stage 2	4 (2.9%)	1 (1.8%)	4 (3.1%)	2 (3.8%)	7 (2.9%)
CKD Stage 3a	0	0	0	1 (11.1%)	1 (2.1%)
Fatigue (疲労)					
CKD Stage 1	0	0	0	1 (7.1%)	1 (2.3%)
CKD Stage 2	1 (0.7%)	0	2 (1.5%)	0	2 (0.8%)
CKD Stage 3a	0	0	0	1 (11.1%)	1 (2.1%)
Malaise (倦怠感)					
CKD Stage 1	1 (6.3%)	0	0	0	0
CKD Stage 2	0	1 (1.8%)	1 (0.8%)	1 (1.9%)	3 (1.3%)
CKD Stage 3a	0	0	0	0	0
Pyrexia (発熱)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	2 (1.5%)	0	0	0	0
CKD Stage 3a	0	0	0	0	0
Chest discomfort (胸部不快感)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	0	1 (0.8%)	0	1 (0.4%)
CKD Stage 3a	0	0	0	0	0
Feeling abnormal (異常感)					
CKD Stage 1	0	0	0	1 (7.1%)	1 (2.3%)
CKD Stage 2	0	0	0	0	0
CKD Stage 3a	0	0	0	0	0
Oedema peripheral (末梢性浮腫)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	0	0	1 (1.9%)	1 (0.4%)
CKD Stage 3a	0	0	0	0	0
Thirst (口渇)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	1 (0.7%)	0	0	0	0
CKD Stage 3a	0	0	0	0	0
Eye disorders (眼障害)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	3 (2.2%)	2 (3.6%)	4 (3.1%)	2 (3.8%)	8 (3.3%)
CKD Stage 3a	1 (3.4%)	0	0	1 (11.1%)	1 (2.1%)
Cataract (白内障)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	1 (0.7%)	0	0	1 (1.9%)	1 (0.4%)
CKD Stage 3a	0	0	0	0	0

System Organ Class Preferred Term Renal function	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
Chalazion (霰粒腫)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	1 (1.8%)	0	0	1 (0.4%)
CKD Stage 3a	0	0	0	1 (11.1%)	1 (2.1%)
Diabetic retinopathy (糖尿病網膜症)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	0	2 (1.5%)	0	2 (0.8%)
CKD Stage 3a	0	0	0	0	0
Glaucoma (緑内障)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	0	2 (1.5%)	0	2 (0.8%)
CKD Stage 3a	0	0	0	0	0
Vitreous floaters (硝子体浮遊物)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	2 (1.5%)	0	0	0	0
CKD Stage 3a	0	0	0	0	0
Dry eye (眼乾燥)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	0	0	0	0
CKD Stage 3a	1 (3.4%)	0	0	0	0
Eye inflammation (眼の炎症)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	0	0	1 (1.9%)	1 (0.4%)
CKD Stage 3a	0	0	0	0	0
Eye swelling (眼部腫脹)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	1 (1.8%)	0	0	1 (0.4%)
CKD Stage 3a	0	0	0	0	0
Macular fibrosis (黄斑線維症)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	0	1 (0.8%)	0	1 (0.4%)
CKD Stage 3a	0	0	0	0	0
Respiratory, thoracic and mediastinal disorders (呼吸器、胸郭および縦隔障害)					
CKD Stage 1	1 (6.3%)	1 (11.1%)	0	0	1 (2.3%)
CKD Stage 2	3 (2.2%)	2 (3.6%)	0	2 (3.8%)	4 (1.7%)
CKD Stage 3a	0	0	0	0	0
Oropharyngeal pain (口腔咽頭痛)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	1 (0.7%)	0	0	2 (3.8%)	2 (0.8%)
CKD Stage 3a	0	0	0	0	0
Upper respiratory tract inflammation (上気道の炎症)					
CKD Stage 1	1 (6.3%)	0	0	0	0

System Organ Class Preferred Term Renal function	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
CKD Stage 2	1 (0.7%)	1 (1.8%)	0	0	1 (0.4%)
CKD Stage 3a	0	0	0	0	0
Rhinitis allergic (アレルギー性鼻炎)					
CKD Stage 1	0	1 (11.1%)	0	0	1 (2.3%)
CKD Stage 2	0	1 (1.8%)	0	0	1 (0.4%)
CKD Stage 3a	0	0	0	0	0
Allergic cough (アレルギー性咳嗽)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	1 (0.7%)	0	0	0	0
CKD Stage 3a	0	0	0	0	0
Asthma (喘息)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	1 (0.7%)	0	0	0	0
CKD Stage 3a	0	0	0	0	0
Cardiac disorders (心臓障害)					
CKD Stage 1	1 (6.3%)	0	0	0	0
CKD Stage 2	0	0	1 (0.8%)	2 (3.8%)	3 (1.3%)
CKD Stage 3a	1 (3.4%)	0	1 (3.6%)	1 (11.1%)	2 (4.3%)
Palpitations (動悸)					
CKD Stage 1	1 (6.3%)	0	0	0	0
CKD Stage 2	0	0	0	1 (1.9%)	1 (0.4%)
CKD Stage 3a	1 (3.4%)	0	1 (3.6%)	0	1 (2.1%)
Atrial fibrillation (心房細動)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	0	0	1 (1.9%)	1 (0.4%)
CKD Stage 3a	0	0	0	0	0
Bradycardia (徐脈)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	0	1 (0.8%)	0	1 (0.4%)
CKD Stage 3a	0	0	0	0	0
Ventricular extrasystoles (心室性期外収縮)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	0	0	0	0
CKD Stage 3a	0	0	0	1 (11.1%)	1 (2.1%)
Vascular disorders (血管障害)					
CKD Stage 1	0	0	1 (4.8%)	0	1 (2.3%)
CKD Stage 2	2 (1.5%)	2 (3.6%)	0	1 (1.9%)	3 (1.3%)
CKD Stage 3a	1 (3.4%)	0	0	0	0
Hypertension (高血圧)					
CKD Stage 1	0	0	1 (4.8%)	0	1 (2.3%)
CKD Stage 2	1 (0.7%)	2 (3.6%)	0	1 (1.9%)	3 (1.3%)
CKD Stage 3a	1 (3.4%)	0	0	0	0

System Organ Class Preferred Term Renal function	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
Arteriosclerosis (動脈硬化症)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	1 (0.7%)	0	0	0	0
CKD Stage 3a	0	0	0	0	0
Ear and labyrinth disorders (耳および迷路障害)					
CKD Stage 1	0	0	0	2 (14.3%)	2 (4.5%)
CKD Stage 2	1 (0.7%)	0	1 (0.8%)	1 (1.9%)	2 (0.8%)
CKD Stage 3a	0	0	1 (3.6%)	0	1 (2.1%)
Vertigo (回転性めまい)					
CKD Stage 1	0	0	0	1 (7.1%)	1 (2.3%)
CKD Stage 2	0	0	0	1 (1.9%)	1 (0.4%)
CKD Stage 3a	0	0	1 (3.6%)	0	1 (2.1%)
Ear congestion (耳閉)					
CKD Stage 1	0	0	0	1 (7.1%)	1 (2.3%)
CKD Stage 2	0	0	0	0	0
CKD Stage 3a	0	0	0	0	0
Eustachian tube stenosis (耳管狭窄)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	1 (0.7%)	0	0	0	0
CKD Stage 3a	0	0	0	0	0
Vertigo positional (頭位性回転性めまい)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	0	1 (0.8%)	0	1 (0.4%)
CKD Stage 3a	0	0	0	0	0
Hepatobiliary disorders (肝胆道系障害)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	3 (2.2%)	0	1 (0.8%)	2 (3.8%)	3 (1.3%)
CKD Stage 3a	0	0	0	0	0
Hepatic steatosis (脂肪肝)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	1 (0.7%)	0	0	1 (1.9%)	1 (0.4%)
CKD Stage 3a	0	0	0	0	0
Gallbladder polyp (胆嚢ポリープ)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	1 (0.7%)	0	0	0	0
CKD Stage 3a	0	0	0	0	0
Hepatic function abnormal (肝機能異常)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	0	1 (0.8%)	0	1 (0.4%)
CKD Stage 3a	0	0	0	0	0

System Organ Class Preferred Term Renal function	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
Hepatomegaly (肝腫大)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	0	0	1 (1.9%)	1 (0.4%)
CKD Stage 3a	0	0	0	0	0
Liver injury (肝損傷)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	1 (0.7%)	0	0	0	0
CKD Stage 3a	0	0	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps) (良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	0	3 (2.3%)	1 (1.9%)	4 (1.7%)
CKD Stage 3a	0	0	1 (3.6%)	0	1 (2.1%)
Bladder cancer (膀胱癌)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	0	1 (0.8%)	0	1 (0.4%)
CKD Stage 3a	0	0	0	0	0
Pancreatic carcinoma metastatic (遠隔転移を伴う膵癌)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	0	0	1 (1.9%)	1 (0.4%)
CKD Stage 3a	0	0	0	0	0
Prostate cancer (前立腺癌)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	0	1 (0.8%)	0	1 (0.4%)
CKD Stage 3a	0	0	0	0	0
Seborrhoeic keratosis (脂漏性角化症)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	0	0	0	0
CKD Stage 3a	0	0	1 (3.6%)	0	1 (2.1%)
Solid pseudopapillary tumour of the pancreas (膵の充実性偽乳頭状腫瘍)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	0	1 (0.8%)	0	1 (0.4%)
CKD Stage 3a	0	0	0	0	0
Psychiatric disorders (精神障害)					
CKD Stage 1	1 (6.3%)	0	0	0	0
CKD Stage 2	0	0	0	0	0
CKD Stage 3a	0	1 (10.0%)	0	1 (11.1%)	2 (4.3%)
Insomnia (不眠症)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	0	0	0	0

System Organ Class Preferred Term Renal function	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
CKD Stage 3a	0	1 (10.0%)	0	1 (11.1%)	2 (4.3%)
Anxiety (不安)					
CKD Stage 1	1 (6.3%)	0	0	0	0
CKD Stage 2	0	0	0	0	0
CKD Stage 3a	0	0	0	0	0
Renal and urinary disorders (腎および尿路障害)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	1 (0.7%)	1 (1.8%)	1 (0.8%)	0	2 (0.8%)
CKD Stage 3a	0	0	0	0	0
Calculus urinary (尿路結石)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	1 (0.7%)	0	0	0	0
CKD Stage 3a	0	0	0	0	0
Diabetic nephropathy (糖尿病性腎症)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	1 (1.8%)	0	0	1 (0.4%)
CKD Stage 3a	0	0	0	0	0
Ureterolithiasis (尿管結石症)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	0	1 (0.8%)	0	1 (0.4%)
CKD Stage 3a	0	0	0	0	0
Reproductive system and breast disorders (生殖系および乳房障害)					
CKD Stage 1	0	1 (11.1%)	0	0	1 (2.3%)
CKD Stage 2	2 (1.5%)	0	0	0	0
CKD Stage 3a	0	0	0	0	0
Benign prostatic hyperplasia (良性前立腺肥大症)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	1 (0.7%)	0	0	0	0
CKD Stage 3a	0	0	0	0	0
Dysmenorrhoea (月経困難症)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	1 (0.7%)	0	0	0	0
CKD Stage 3a	0	0	0	0	0
Metrorrhagia (不正子宮出血)					
CKD Stage 1	0	1 (11.1%)	0	0	1 (2.3%)
CKD Stage 2	0	0	0	0	0
CKD Stage 3a	0	0	0	0	0
Prostatitis (前立腺炎)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	1 (0.7%)	0	0	0	0
CKD Stage 3a	0	0	0	0	0

System Organ Class Preferred Term Renal function	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
Blood and lymphatic system disorders (血液およびリンパ系障害)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	0	1 (0.8%)	0	1 (0.4%)
CKD Stage 3a	0	0	0	0	0
Anaemia (貧血)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	0	1 (0.8%)	0	1 (0.4%)
CKD Stage 3a	0	0	0	0	0
Endocrine disorders (内分泌障害)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	0	0	0	0
CKD Stage 3a	0	0	0	1 (11.1%)	1 (2.1%)
Thyroid cyst (甲状腺嚢腫)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	0	0	0	0
CKD Stage 3a	0	0	0	1 (11.1%)	1 (2.1%)
Thyroid mass (甲状腺腫瘤)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	0	0	0	0
CKD Stage 3a	0	0	0	1 (11.1%)	1 (2.1%)
Social circumstances (社会環境)					
CKD Stage 1	1 (6.3%)	0	0	0	0
CKD Stage 2	0	0	0	0	0
CKD Stage 3a	0	0	0	0	0
Menopause (閉経)					
CKD Stage 1	1 (6.3%)	0	0	0	0
CKD Stage 2	0	0	0	0	0
CKD Stage 3a	0	0	0	0	0
Surgical and medical procedures (外科および内科処置)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	0	1 (0.8%)	0	1 (0.4%)
CKD Stage 3a	0	0	0	0	0
Blepharoplasty (眼瞼形成)					
CKD Stage 1	0	0	0	0	0
CKD Stage 2	0	0	1 (0.8%)	0	1 (0.4%)

System Organ Class Preferred Term Renal function	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
CKD Stage 3a	0	0	0	0	0

- Abbreviations: bid, Twice a day; AE, Adverse event; TEAE, Treatment Emergent AE; eGFR, Estimated Glomerular Filtration Rate; CKD, Chronic Kidney Disease
- CKD Stage 1 includes subjects with eGFR >= 90 mL/min/1.73m2, CKD Stage 2 includes subjects with eGFR >= 60 to < 90 mL/min/1.73m2, CKD Stage 3a includes subjects with eGFR >= 45 to < 60 mL/min/1.73m2.
- All adverse events were coded using MedDRA dictionary version 20.1.
- Percentages are based on "Number of patients".

Control No:<<t-s-164-subae-24wdb.sas, 2020-03-06T00:12:43>>

Table S-165 Subgroup Analysis of Treatment Emergent Adverse Events by Hepatic Parameter Abnormality, System Organ Class and Preferred Term in 24-Week Double-blind Period with Monotherapy (PXL008-014, PXL008-018; Safety Population)

System Organ Class Preferred Term Hepatic parameter abnormality	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
Number of patients					
Yes	31	14	24	14	52
No	151	61	156	61	278
Any TEAE					
Yes	14 (45.2%)	9 (64.3%)	14 (58.3%)	12 (85.7%)	35 (67.3%)
No	85 (56.3%)	42 (68.9%)	79 (50.6%)	43 (70.5%)	164 (59.0%)
Infections and infestations (感染症および寄生虫症)					
Yes	5 (16.1%)	5 (35.7%)	10 (41.7%)	5 (35.7%)	20 (38.5%)
No	27 (17.9%)	22 (36.1%)	40 (25.6%)	21 (34.4%)	83 (29.9%)
Nasopharyngitis (上咽頭炎)					
Yes	2 (6.5%)	3 (21.4%)	6 (25.0%)	2 (14.3%)	11 (21.2%)
No	18 (11.9%)	17 (27.9%)	27 (17.3%)	16 (26.2%)	60 (21.6%)
Bronchitis (気管支炎)					
Yes	1 (3.2%)	0	0	1 (7.1%)	1 (1.9%)
No	0	3 (4.9%)	2 (1.3%)	0	5 (1.8%)
Gastroenteritis (胃腸炎)					
Yes	2 (6.5%)	1 (7.1%)	1 (4.2%)	0	2 (3.8%)
No	0	1 (1.6%)	1 (0.6%)	0	2 (0.7%)
Pharyngitis (咽頭炎)					
Yes	0	1 (7.1%)	1 (4.2%)	0	2 (3.8%)
No	2 (1.3%)	0	2 (1.3%)	0	2 (0.7%)
Periodontitis (歯周炎)					
Yes	0	0	0	0	0
No	2 (1.3%)	1 (1.6%)	1 (0.6%)	1 (1.6%)	3 (1.1%)
Influenza (インフルエンザ)					
Yes	0	0	0	1 (7.1%)	1 (1.9%)
No	0	0	3 (1.9%)	0	3 (1.1%)
Upper respiratory tract infection (上気道感染)					
Yes	0	0	0	0	0
No	2 (1.3%)	0	1 (0.6%)	1 (1.6%)	2 (0.7%)
Conjunctivitis (結膜炎)					
Yes	0	0	0	0	0
No	0	0	3 (1.9%)	0	3 (1.1%)
Cystitis (膀胱炎)					
Yes	0	0	0	0	0
No	1 (0.7%)	2 (3.3%)	0	0	2 (0.7%)
Otitis externa (外耳炎)					
Yes	0	0	0	0	0
No	1 (0.7%)	0	1 (0.6%)	1 (1.6%)	2 (0.7%)

System Organ Class Preferred Term Hepatic parameter abnormality	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
Gastroenteritis viral (ウイルス性胃腸炎)					
Yes	1 (3.2%)	0	0	0	0
No	0	0	0	1 (1.6%)	1 (0.4%)
Herpes zoster (帯状疱疹)					
Yes	0	0	0	1 (7.1%)	1 (1.9%)
No	1 (0.7%)	0	0	0	0
Infected dermal cyst (感染性皮膚嚢腫)					
Yes	0	0	0	0	0
No	1 (0.7%)	0	1 (0.6%)	0	1 (0.4%)
Oral herpes (口腔ヘルペス)					
Yes	1 (3.2%)	0	0	0	0
No	1 (0.7%)	0	0	0	0
Asymptomatic bacteriuria (無症候性細菌尿)					
Yes	0	0	1 (4.2%)	0	1 (1.9%)
No	0	0	0	0	0
Bronchitis bacterial (細菌性気管支炎)					
Yes	0	0	1 (4.2%)	0	1 (1.9%)
No	0	0	0	0	0
Conjunctivitis bacterial (細菌性結膜炎)					
Yes	0	0	0	0	0
No	0	0	0	1 (1.6%)	1 (0.4%)
Gingivitis (歯肉炎)					
Yes	0	0	0	0	0
No	1 (0.7%)	0	0	0	0
Helicobacter infection (ヘリコバクター感染)					
Yes	0	0	0	0	0
No	1 (0.7%)	0	0	0	0
Hordeolum (麦粒腫)					
Yes	0	0	0	0	0
No	0	0	1 (0.6%)	0	1 (0.4%)
Parotitis (耳下腺炎)					
Yes	0	0	0	1 (7.1%)	1 (1.9%)
No	0	0	0	0	0
Pericoronitis (歯冠周囲炎)					
Yes	0	0	0	0	0
No	0	0	0	1 (1.6%)	1 (0.4%)
Pharyngitis streptococcal (レンサ球菌性咽頭炎)					
Yes	0	0	0	0	0
No	1 (0.7%)	0	0	0	0

System Organ Class Preferred Term Hepatic parameter abnormality	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
Pulpitis dental (歯髄炎)					
Yes	0	0	0	0	0
No	0	1 (1.6%)	0	0	1 (0.4%)
Tooth abscess (歯膿瘍)					
Yes	0	0	0	0	0
No	1 (0.7%)	0	0	0	0
Gastrointestinal disorders (胃腸障害)					
Yes	1 (3.2%)	4 (28.6%)	2 (8.3%)	4 (28.6%)	10 (19.2%)
No	19 (12.6%)	7 (11.5%)	24 (15.4%)	20 (32.8%)	51 (18.3%)
Diarrhoea (下痢)					
Yes	0	3 (21.4%)	0	1 (7.1%)	4 (7.7%)
No	1 (0.7%)	0	5 (3.2%)	5 (8.2%)	10 (3.6%)
Abdominal discomfort (腹部不快感)					
Yes	0	1 (7.1%)	0	1 (7.1%)	2 (3.8%)
No	0	0	3 (1.9%)	6 (9.8%)	9 (3.2%)
Vomiting (嘔吐)					
Yes	1 (3.2%)	0	0	1 (7.1%)	1 (1.9%)
No	3 (2.0%)	0	1 (0.6%)	3 (4.9%)	4 (1.4%)
Nausea (悪心)					
Yes	0	1 (7.1%)	0	0	1 (1.9%)
No	1 (0.7%)	0	1 (0.6%)	5 (8.2%)	6 (2.2%)
Dental caries (齲歯)					
Yes	0	0	0	0	0
No	4 (2.6%)	0	2 (1.3%)	1 (1.6%)	3 (1.1%)
Constipation (便秘)					
Yes	0	0	1 (4.2%)	0	1 (1.9%)
No	2 (1.3%)	1 (1.6%)	1 (0.6%)	1 (1.6%)	3 (1.1%)
Abdominal pain upper (上腹部痛)					
Yes	0	0	0	0	0
No	1 (0.7%)	2 (3.3%)	1 (0.6%)	0	3 (1.1%)
Gastrooesophageal reflux disease (胃食道逆流性疾患)					
Yes	0	0	0	1 (7.1%)	1 (1.9%)
No	1 (0.7%)	1 (1.6%)	1 (0.6%)	0	2 (0.7%)
Dyspepsia (消化不良)					
Yes	0	0	0	0	0
No	0	1 (1.6%)	1 (0.6%)	1 (1.6%)	3 (1.1%)
Gastritis (胃炎)					
Yes	0	0	1 (4.2%)	0	1 (1.9%)
No	0	1 (1.6%)	1 (0.6%)	0	2 (0.7%)
Periodontal disease (歯周病)					
Yes	0	0	1 (4.2%)	0	1 (1.9%)
No	1 (0.7%)	1 (1.6%)	0	0	1 (0.4%)

System Organ Class Preferred Term Hepatic parameter abnormality	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
Abdominal distension (腹部膨満)					
Yes	0	0	0	0	0
No	0	0	1 (0.6%)	1 (1.6%)	2 (0.7%)
Abdominal pain (腹痛)					
Yes	0	0	0	0	0
No	0	0	2 (1.3%)	0	2 (0.7%)
Chronic gastritis (慢性胃炎)					
Yes	0	0	0	0	0
No	0	0	2 (1.3%)	0	2 (0.7%)
Duodenal ulcer (十二指腸潰瘍)					
Yes	0	0	0	0	0
No	2 (1.3%)	0	0	0	0
Faeces soft (軟便)					
Yes	0	0	0	0	0
No	2 (1.3%)	0	0	0	0
Stomatitis (口内炎)					
Yes	0	0	0	0	0
No	0	0	1 (0.6%)	1 (1.6%)	2 (0.7%)
Abdominal pain lower (下腹部痛)					
Yes	0	0	0	0	0
No	1 (0.7%)	0	0	0	0
Abnormal faeces (異常便)					
Yes	0	0	0	0	0
No	0	0	1 (0.6%)	0	1 (0.4%)
Duodenal polyp (十二指腸ポリープ)					
Yes	0	0	0	0	0
No	0	1 (1.6%)	0	0	1 (0.4%)
Duodenitis (十二指腸炎)					
Yes	0	0	0	0	0
No	0	1 (1.6%)	0	0	1 (0.4%)
Enteritis (小腸炎)					
Yes	0	0	0	0	0
No	0	0	0	1 (1.6%)	1 (0.4%)
Enterocolitis (腸炎)					
Yes	0	0	0	0	0
No	1 (0.7%)	0	0	0	0
Epigastric discomfort (心窩部不快感)					
Yes	0	0	0	0	0
No	0	0	1 (0.6%)	0	1 (0.4%)
Gastric polyps (胃ポリープ)					
Yes	0	0	0	0	0
No	1 (0.7%)	0	0	0	0
Ileus (イレウス)					
Yes	0	0	0	0	0

System Organ Class Preferred Term Hepatic parameter abnormality	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
No	0	0	1 (0.6%)	0	1 (0.4%)
Large intestine polyp (大腸ポリープ)					
Yes	0	0	0	0	0
No	0	0	1 (0.6%)	0	1 (0.4%)
Loose tooth (弛緩歯)					
Yes	0	0	0	0	0
No	0	0	1 (0.6%)	0	1 (0.4%)
Melaena (メレナ)					
Yes	0	0	0	0	0
No	1 (0.7%)	0	0	0	0
Tooth loss (歯の脱落)					
Yes	0	0	0	0	0
No	1 (0.7%)	0	0	0	0
Metabolism and nutrition disorders (代謝および栄養障害)					
Yes	5 (16.1%)	1 (7.1%)	3 (12.5%)	3 (21.4%)	7 (13.5%)
No	16 (10.6%)	7 (11.5%)	6 (3.8%)	2 (3.3%)	15 (5.4%)
Hyperglycaemia (高血糖)					
Yes	4 (12.9%)	0	0	1 (7.1%)	1 (1.9%)
No	12 (7.9%)	3 (4.9%)	1 (0.6%)	0	4 (1.4%)
Hypoglycaemia (低血糖)					
Yes	0	1 (7.1%)	1 (4.2%)	2 (14.3%)	4 (7.7%)
No	2 (1.3%)	4 (6.6%)	4 (2.6%)	2 (3.3%)	10 (3.6%)
Dyslipidaemia (脂質異常症)					
Yes	0	0	2 (8.3%)	0	2 (3.8%)
No	3 (2.0%)	0	0	0	0
Hyperuricaemia (高尿酸血症)					
Yes	1 (3.2%)	0	0	0	0
No	0	0	1 (0.6%)	0	1 (0.4%)
Musculoskeletal and connective tissue disorders (筋骨格系および結合組織障害)					
Yes	1 (3.2%)	3 (21.4%)	0	0	3 (5.8%)
No	16 (10.6%)	6 (9.8%)	11 (7.1%)	5 (8.2%)	22 (7.9%)
Arthralgia (関節痛)					
Yes	0	1 (7.1%)	0	0	1 (1.9%)
No	4 (2.6%)	0	1 (0.6%)	1 (1.6%)	2 (0.7%)
Back pain (背部痛)					
Yes	0	1 (7.1%)	0	0	1 (1.9%)
No	0	3 (4.9%)	1 (0.6%)	1 (1.6%)	5 (1.8%)
Muscle spasms (筋痙縮)					
Yes	0	0	0	0	0

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No	3 (2.0%)	0	3 (1.9%)	0	3 (1.1%)
Periarthritis (関節周囲炎)					
Yes	0	0	0	0	0
No	2 (1.3%)	0	1 (0.6%)	0	1 (0.4%)
Musculoskeletal pain (筋骨格痛)					
Yes	0	0	0	0	0
No	1 (0.7%)	0	0	1 (1.6%)	1 (0.4%)
Musculoskeletal stiffness (筋骨格硬直)					
Yes	0	0	0	0	0
No	1 (0.7%)	1 (1.6%)	0	0	1 (0.4%)
Osteoarthritis (変形性関節症)					
Yes	0	0	0	0	0
No	1 (0.7%)	0	1 (0.6%)	0	1 (0.4%)
Plantar fasciitis (足底筋膜炎)					
Yes	1 (3.2%)	0	0	0	0
No	1 (0.7%)	0	0	0	0
Arthritis (関節炎)					
Yes	0	1 (7.1%)	0	0	1 (1.9%)
No	0	0	0	0	0
Fasciitis (筋膜炎)					
Yes	0	0	0	0	0
No	1 (0.7%)	0	0	0	0
Intervertebral disc degeneration (椎間板変性症)					
Yes	0	0	0	0	0
No	0	0	1 (0.6%)	0	1 (0.4%)
Intervertebral disc protrusion (椎間板突出)					
Yes	0	1 (7.1%)	0	0	1 (1.9%)
No	0	0	0	0	0
Joint swelling (関節腫脹)					
Yes	0	0	0	0	0
No	1 (0.7%)	0	0	0	0
Mastication disorder (咀嚼障害)					
Yes	0	0	0	0	0
No	0	0	0	1 (1.6%)	1 (0.4%)
Muscular weakness (筋力低下)					
Yes	0	0	0	0	0
No	0	0	1 (0.6%)	0	1 (0.4%)
Musculoskeletal chest pain (筋骨格系胸痛)					
Yes	0	0	0	0	0
No	0	1 (1.6%)	0	0	1 (0.4%)
Myalgia (筋肉痛)					

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Yes	0	0	0	0	0
No	0	0	1 (0.6%)	0	1 (0.4%)
Neck pain (頚部痛)					
Yes	0	0	0	0	0
No	0	0	0	1 (1.6%)	1 (0.4%)
Osteoporosis (骨粗鬆症)					
Yes	0	0	0	0	0
No	1 (0.7%)	0	0	0	0
Pain in extremity (四肢痛)					
Yes	0	0	0	0	0
No	0	1 (1.6%)	0	0	1 (0.4%)
Spinal osteoarthritis (変形性脊椎症)					
Yes	0	0	0	0	0
No	0	0	1 (0.6%)	0	1 (0.4%)
Spondylolisthesis (脊椎すべり症)					
Yes	0	0	0	0	0
No	1 (0.7%)	0	0	0	0
Temporomandibular joint syndrome (顎関節症候群)					
Yes	0	0	0	0	0
No	0	0	0	1 (1.6%)	1 (0.4%)
Injury, poisoning and procedural complications (傷害、中毒および処置合併症)					
Yes	1 (3.2%)	1 (7.1%)	0	2 (14.3%)	3 (5.8%)
No	5 (3.3%)	4 (6.6%)	8 (5.1%)	4 (6.6%)	16 (5.8%)
Contusion (挫傷)					
Yes	1 (3.2%)	1 (7.1%)	0	0	1 (1.9%)
No	0	1 (1.6%)	1 (0.6%)	1 (1.6%)	3 (1.1%)
Arthropod sting (節足動物刺傷)					
Yes	0	0	0	0	0
No	0	2 (3.3%)	0	2 (3.3%)	4 (1.4%)
Hand fracture (手骨折)					
Yes	0	1 (7.1%)	0	0	1 (1.9%)
No	0	0	0	1 (1.6%)	1 (0.4%)
Ligament sprain (靱帯捻挫)					
Yes	0	0	0	1 (7.1%)	1 (1.9%)
No	0	0	1 (0.6%)	0	1 (0.4%)
Radius fracture (橈骨骨折)					
Yes	0	0	0	1 (7.1%)	1 (1.9%)
No	0	0	1 (0.6%)	0	1 (0.4%)
Skin abrasion (皮膚擦過傷)					
Yes	0	0	0	0	0

System Organ Class Preferred Term Hepatic parameter abnormality	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
No	0	0	2 (1.3%)	0	2 (0.7%)
Arthropod bite (節足動物咬傷)					
Yes	0	0	0	0	0
No	1 (0.7%)	0	0	0	0
Bone contusion (骨挫傷)					
Yes	0	0	0	0	0
No	0	0	0	1 (1.6%)	1 (0.4%)
Clavicle fracture (鎖骨骨折)					
Yes	0	0	0	0	0
No	0	0	1 (0.6%)	0	1 (0.4%)
Fall (転倒)					
Yes	0	0	0	0	0
No	0	0	0	1 (1.6%)	1 (0.4%)
Femur fracture (大腿骨骨折)					
Yes	0	0	0	0	0
No	0	0	1 (0.6%)	0	1 (0.4%)
Limb injury (四肢損傷)					
Yes	0	0	0	0	0
No	1 (0.7%)	0	0	0	0
Lower limb fracture (下肢骨折)					
Yes	0	0	0	0	0
No	1 (0.7%)	0	0	0	0
Meniscus injury (半月板損傷)					
Yes	0	0	0	0	0
No	1 (0.7%)	0	0	0	0
Muscle rupture (筋断裂)					
Yes	0	0	0	0	0
No	1 (0.7%)	0	0	0	0
Post procedural haemorrhage (処置後出血)					
Yes	0	0	0	0	0
No	0	0	1 (0.6%)	0	1 (0.4%)
Rib fracture (肋骨骨折)					
Yes	0	0	0	0	0
No	0	1 (1.6%)	0	0	1 (0.4%)
Thermal burn (熱傷)					
Yes	0	0	0	0	0
No	0	0	1 (0.6%)	0	1 (0.4%)
Skin and subcutaneous tissue disorders (皮膚および皮下組織障害)					
Yes	1 (3.2%)	1 (7.1%)	1 (4.2%)	1 (7.1%)	3 (5.8%)
No	11 (7.3%)	2 (3.3%)	4 (2.6%)	4 (6.6%)	10 (3.6%)
Eczema (湿疹)					

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Yes	0	0	0	1 (7.1%)	1 (1.9%)
No	2 (1.3%)	2 (3.3%)	2 (1.3%)	2 (3.3%)	6 (2.2%)
Dermatitis contact (接触皮膚炎)					
Yes	0	0	1 (4.2%)	0	1 (1.9%)
No	1 (0.7%)	0	0	0	0
Dyshidrotic eczema (異汗性湿疹)					
Yes	0	0	0	0	0
No	1 (0.7%)	0	1 (0.6%)	0	1 (0.4%)
Ingrowing nail (嵌入爪)					
Yes	0	0	0	0	0
No	1 (0.7%)	0	0	1 (1.6%)	1 (0.4%)
Miliaria (汗疹)					
Yes	0	1 (7.1%)	0	0	1 (1.9%)
No	1 (0.7%)	0	0	0	0
Alopecia areata (円形脱毛症)					
Yes	0	0	0	0	0
No	1 (0.7%)	0	0	0	0
Drug eruption (薬疹)					
Yes	0	0	0	0	0
No	1 (0.7%)	0	0	0	0
Dry skin (皮膚乾燥)					
Yes	0	0	0	0	0
No	0	0	1 (0.6%)	0	1 (0.4%)
Eczema asteatotic (皮脂欠乏性湿疹)					
Yes	1 (3.2%)	0	0	0	0
No	0	0	0	0	0
Pruritus (そう痒症)					
Yes	0	0	0	0	0
No	1 (0.7%)	0	0	0	0
Pustular psoriasis (膿疱性乾癬)					
Yes	0	0	0	0	0
No	1 (0.7%)	0	0	0	0
Rash (発疹)					
Yes	0	0	0	0	0
No	1 (0.7%)	0	0	0	0
Toxic skin eruption (中毒性皮疹)					
Yes	1 (3.2%)	0	0	0	0
No	0	0	0	0	0
Urticaria (蕁麻疹)					
Yes	0	0	0	0	0
No	1 (0.7%)	0	0	0	0
Xanthoma (黄色腫)					
Yes	0	0	0	0	0
No	0	0	0	1 (1.6%)	1 (0.4%)

System Organ Class Preferred Term Hepatic parameter abnormality	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
Nervous system disorders (神経系障害)					
Yes	1 (3.2%)	1 (7.1%)	2 (8.3%)	1 (7.1%)	4 (7.7%)
No	9 (6.0%)	5 (8.2%)	5 (3.2%)	0	10 (3.6%)
Dizziness (浮動性めまい)					
Yes	1 (3.2%)	0	1 (4.2%)	0	1 (1.9%)
No	3 (2.0%)	1 (1.6%)	0	0	1 (0.4%)
Headache (頭痛)					
Yes	0	0	0	0	0
No	2 (1.3%)	2 (3.3%)	1 (0.6%)	0	3 (1.1%)
Cervical radiculopathy (頚髄神経根障害)					
Yes	0	0	0	0	0
No	1 (0.7%)	0	1 (0.6%)	0	1 (0.4%)
Dizziness postural (体位性めまい)					
Yes	0	0	0	0	0
No	1 (0.7%)	1 (1.6%)	0	0	1 (0.4%)
Presyncope (失神寸前の状態)					
Yes	0	0	1 (4.2%)	0	1 (1.9%)
No	0	0	1 (0.6%)	0	1 (0.4%)
Carpal tunnel syndrome (手根管症候群)					
Yes	0	0	0	0	0
No	0	0	1 (0.6%)	0	1 (0.4%)
Dysgeusia (味覚異常)					
Yes	0	0	0	1 (7.1%)	1 (1.9%)
No	0	0	0	0	0
Hypoaesthesia (感覚鈍麻)					
Yes	0	0	0	0	0
No	1 (0.7%)	0	0	0	0
IVth nerve disorder (第 4 脳神経障害)					
Yes	0	0	0	0	0
No	0	1 (1.6%)	0	0	1 (0.4%)
Intercostal neuralgia (肋間神経痛)					
Yes	0	0	0	0	0
No	1 (0.7%)	0	0	0	0
Loss of consciousness (意識消失)					
Yes	0	0	0	0	0
No	0	0	1 (0.6%)	0	1 (0.4%)
Orthostatic intolerance (起立不耐性)					
Yes	0	0	0	0	0
No	0	1 (1.6%)	0	0	1 (0.4%)
Spondylitic myelopathy (脊椎炎性脊髄症)					

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Yes	0	0	0	0	0
No	0	0	1 (0.6%)	0	1 (0.4%)
Thoracic outlet syndrome (胸郭出口症候群)					
Yes	0	1 (7.1%)	0	0	1 (1.9%)
No	0	0	0	0	0
Investigations (臨床検査)					
Yes	3 (9.7%)	1 (7.1%)	2 (8.3%)	1 (7.1%)	4 (7.7%)
No	4 (2.6%)	4 (6.6%)	2 (1.3%)	5 (8.2%)	11 (4.0%)
Culture urine positive (尿培養陽性)					
Yes	0	0	0	1 (7.1%)	1 (1.9%)
No	1 (0.7%)	1 (1.6%)	0	3 (4.9%)	4 (1.4%)
Blood bilirubin increased (血中ビリルビン増加)					
Yes	2 (6.5%)	0	0	0	0
No	0	0	0	0	0
Blood creatine phosphokinase increased (血中クレアチンホスホキナーゼ増加)					
Yes	1 (3.2%)	0	0	0	0
No	1 (0.7%)	0	0	0	0
Gamma-glutamyltransferase increased (γ－グルタミルトランスフェラーゼ増加)					
Yes	1 (3.2%)	0	0	0	0
No	0	0	0	1 (1.6%)	1 (0.4%)
Urine albumin/creatinine ratio increased (尿中アルブミン／クレアチニン比増加)					
Yes	0	0	0	0	0
No	1 (0.7%)	0	1 (0.6%)	0	1 (0.4%)
Activated partial thromboplastin time prolonged (活性化部分トロンボプラスチン時間延長)					
Yes	0	0	0	0	0
No	0	1 (1.6%)	0	0	1 (0.4%)
Alanine aminotransferase increased (アラニンアミノトランスフェラーゼ増加)					
Yes	1 (3.2%)	0	0	0	0
No	0	0	0	0	0
Aspartate aminotransferase increased (アスパラギン酸アミノトランスフェラーゼ増加)					
Yes	1 (3.2%)	0	0	0	0
No	0	0	0	0	0

System Organ Class Preferred Term Hepatic parameter abnormality	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
Blood glucagon increased (血中グルカゴン増加)					
Yes	0	0	0	1 (7.1%)	1 (1.9%)
No	0	0	0	0	0
Blood pressure increased (血圧上昇)					
Yes	0	0	0	0	0
No	1 (0.7%)	0	0	0	0
C-reactive protein increased (Ｃ－反応性蛋白増加)					
Yes	0	0	1 (4.2%)	0	1 (1.9%)
No	0	0	0	0	0
Electrocardiogram T wave inversion (心電図Ｔ波逆転)					
Yes	0	0	0	0	0
No	0	0	0	1 (1.6%)	1 (0.4%)
Eosinophil count increased (好酸球数増加)					
Yes	0	0	0	0	0
No	0	1 (1.6%)	0	0	1 (0.4%)
International normalised ratio increased (国際標準比増加)					
Yes	0	0	0	0	0
No	0	1 (1.6%)	0	0	1 (0.4%)
Lipase increased (リパーゼ増加)					
Yes	0	0	0	0	0
No	0	1 (1.6%)	0	0	1 (0.4%)
Liver function test increased (肝機能検査値上昇)					
Yes	0	0	1 (4.2%)	0	1 (1.9%)
No	0	0	0	0	0
Neutrophil count decreased (好中球数減少)					
Yes	0	0	0	0	0
No	0	0	1 (0.6%)	0	1 (0.4%)
Occult blood (便潜血)					
Yes	0	1 (7.1%)	0	0	1 (1.9%)
No	0	0	0	0	0
General disorders and administration site conditions (一般・全身障害および投与部位の状態)					
Yes	2 (6.5%)	0	0	1 (7.1%)	1 (1.9%)
No	3 (2.0%)	1 (1.6%)	4 (2.6%)	4 (6.6%)	9 (3.2%)
Fatigue (疲労)					

System Organ Class Preferred Term Hepatic parameter abnormality	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
Yes	0	0	0	0	0
No	1 (0.7%)	0	2 (1.3%)	2 (3.3%)	4 (1.4%)
Malaise (倦怠感)					
Yes	0	0	0	0	0
No	1 (0.7%)	1 (1.6%)	1 (0.6%)	1 (1.6%)	3 (1.1%)
Pyrexia (発熱)					
Yes	1 (3.2%)	0	0	0	0
No	1 (0.7%)	0	0	0	0
Chest discomfort (胸部不快感)					
Yes	0	0	0	0	0
No	0	0	1 (0.6%)	0	1 (0.4%)
Feeling abnormal (異常感)					
Yes	0	0	0	0	0
No	0	0	0	1 (1.6%)	1 (0.4%)
Oedema peripheral (末梢性浮腫)					
Yes	0	0	0	1 (7.1%)	1 (1.9%)
No	0	0	0	0	0
Thirst (口渇)					
Yes	1 (3.2%)	0	0	0	0
No	0	0	0	0	0
Eye disorders (眼障害)					
Yes	1 (3.2%)	0	0	1 (7.1%)	1 (1.9%)
No	3 (2.0%)	2 (3.3%)	4 (2.6%)	2 (3.3%)	8 (2.9%)
Cataract (白内障)					
Yes	0	0	0	0	0
No	1 (0.7%)	0	0	1 (1.6%)	1 (0.4%)
Chalazion (霰粒腫)					
Yes	0	0	0	0	0
No	0	1 (1.6%)	0	1 (1.6%)	2 (0.7%)
Diabetic retinopathy (糖尿病網膜症)					
Yes	0	0	0	0	0
No	0	0	2 (1.3%)	0	2 (0.7%)
Glaucoma (緑内障)					
Yes	0	0	0	0	0
No	0	0	2 (1.3%)	0	2 (0.7%)
Vitreous floaters (硝子体浮遊物)					
Yes	1 (3.2%)	0	0	0	0
No	1 (0.7%)	0	0	0	0
Dry eye (眼乾燥)					
Yes	0	0	0	0	0
No	1 (0.7%)	0	0	0	0
Eye inflammation (眼の炎症)					
Yes	0	0	0	1 (7.1%)	1 (1.9%)

System Organ Class Preferred Term Hepatic parameter abnormality	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
No	0	0	0	0	0
Eye swelling (眼部腫脹)					
Yes	0	0	0	0	0
No	0	1 (1.6%)	0	0	1 (0.4%)
Macular fibrosis (黄斑線維症)					
Yes	0	0	0	0	0
No	0	0	1 (0.6%)	0	1 (0.4%)
Respiratory, thoracic and mediastinal disorders (呼吸器、胸郭および縦隔障害)					
Yes	0	0	0	0	0
No	4 (2.6%)	3 (4.9%)	0	2 (3.3%)	5 (1.8%)
Oropharyngeal pain (口腔咽頭痛)					
Yes	0	0	0	0	0
No	1 (0.7%)	0	0	2 (3.3%)	2 (0.7%)
Upper respiratory tract inflammation (上気道の炎症)					
Yes	0	0	0	0	0
No	2 (1.3%)	1 (1.6%)	0	0	1 (0.4%)
Rhinitis allergic (アレルギー性鼻炎)					
Yes	0	0	0	0	0
No	0	2 (3.3%)	0	0	2 (0.7%)
Allergic cough (アレルギー性咳嗽)					
Yes	0	0	0	0	0
No	1 (0.7%)	0	0	0	0
Asthma (喘息)					
Yes	0	0	0	0	0
No	1 (0.7%)	0	0	0	0
Cardiac disorders (心臓障害)					
Yes	0	0	0	0	0
No	2 (1.3%)	0	2 (1.3%)	3 (4.9%)	5 (1.8%)
Palpitations (動悸)					
Yes	0	0	0	0	0
No	2 (1.3%)	0	1 (0.6%)	1 (1.6%)	2 (0.7%)
Atrial fibrillation (心房細動)					
Yes	0	0	0	0	0
No	0	0	0	1 (1.6%)	1 (0.4%)
Bradycardia (徐脈)					
Yes	0	0	0	0	0
No	0	0	1 (0.6%)	0	1 (0.4%)
Ventricular extrasystoles (心室性期外収縮)					
Yes	0	0	0	0	0

System Organ Class Preferred Term Hepatic parameter abnormality	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
No	0	0	0	1 (1.6%)	1 (0.4%)
Vascular disorders (血管障害)					
Yes	0	1 (7.1%)	0	0	1 (1.9%)
No	3 (2.0%)	1 (1.6%)	1 (0.6%)	1 (1.6%)	3 (1.1%)
Hypertension (高血圧)					
Yes	0	1 (7.1%)	0	0	1 (1.9%)
No	2 (1.3%)	1 (1.6%)	1 (0.6%)	1 (1.6%)	3 (1.1%)
Arteriosclerosis (動脈硬化症)					
Yes	0	0	0	0	0
No	1 (0.7%)	0	0	0	0
Ear and labyrinth disorders (耳および迷路障害)					
Yes	0	0	0	0	0
No	1 (0.7%)	0	2 (1.3%)	3 (4.9%)	5 (1.8%)
Vertigo (回転性めまい)					
Yes	0	0	0	0	0
No	0	0	1 (0.6%)	2 (3.3%)	3 (1.1%)
Ear congestion (耳閉)					
Yes	0	0	0	0	0
No	0	0	0	1 (1.6%)	1 (0.4%)
Eustachian tube stenosis (耳管狭窄)					
Yes	0	0	0	0	0
No	1 (0.7%)	0	0	0	0
Vertigo positional (頭位性回転性めまい)					
Yes	0	0	0	0	0
No	0	0	1 (0.6%)	0	1 (0.4%)
Hepatobiliary disorders (肝胆道系障害)					
Yes	1 (3.2%)	0	1 (4.2%)	1 (7.1%)	2 (3.8%)
No	2 (1.3%)	0	0	1 (1.6%)	1 (0.4%)
Hepatic steatosis (脂肪肝)					
Yes	0	0	0	1 (7.1%)	1 (1.9%)
No	1 (0.7%)	0	0	0	0
Gallbladder polyp (胆嚢ポリープ)					
Yes	1 (3.2%)	0	0	0	0
No	0	0	0	0	0
Hepatic function abnormal (肝機能異常)					
Yes	0	0	1 (4.2%)	0	1 (1.9%)
No	0	0	0	0	0
Hepatomegaly (肝腫大)					

System Organ Class Preferred Term Hepatic parameter abnormality	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
Yes	0	0	0	0	0
No	0	0	0	1 (1.6%)	1 (0.4%)
Liver injury (肝損傷)					
Yes	0	0	0	0	0
No	1 (0.7%)	0	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps) (良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）)					
Yes	0	0	0	0	0
No	0	0	4 (2.6%)	1 (1.6%)	5 (1.8%)
Bladder cancer (膀胱癌)					
Yes	0	0	0	0	0
No	0	0	1 (0.6%)	0	1 (0.4%)
Pancreatic carcinoma metastatic (遠隔転移を伴う膵癌)					
Yes	0	0	0	0	0
No	0	0	0	1 (1.6%)	1 (0.4%)
Prostate cancer (前立腺癌)					
Yes	0	0	0	0	0
No	0	0	1 (0.6%)	0	1 (0.4%)
Seborrhoeic keratosis (脂漏性角化症)					
Yes	0	0	0	0	0
No	0	0	1 (0.6%)	0	1 (0.4%)
Solid pseudopapillary tumour of the pancreas (膵の充実性偽乳頭状腫瘍)					
Yes	0	0	0	0	0
No	0	0	1 (0.6%)	0	1 (0.4%)
Psychiatric disorders (精神障害)					
Yes	0	0	0	0	0
No	1 (0.7%)	1 (1.6%)	0	1 (1.6%)	2 (0.7%)
Insomnia (不眠症)					
Yes	0	0	0	0	0
No	0	1 (1.6%)	0	1 (1.6%)	2 (0.7%)
Anxiety (不安)					
Yes	0	0	0	0	0
No	1 (0.7%)	0	0	0	0
Renal and urinary disorders (腎および尿路障害)					
Yes	0	0	0	0	0
No	1 (0.7%)	1 (1.6%)	1 (0.6%)	0	2 (0.7%)
Calculus urinary (尿路結石)					

System Organ Class Preferred Term Hepatic parameter abnormality	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
Yes	0	0	0	0	0
No	1 (0.7%)	0	0	0	0
Diabetic nephropathy (糖尿病性腎症)					
Yes	0	0	0	0	0
No	0	1 (1.6%)	0	0	1 (0.4%)
Ureterolithiasis (尿管結石症)					
Yes	0	0	0	0	0
No	0	0	1 (0.6%)	0	1 (0.4%)
Reproductive system and breast disorders (生殖系および乳房障害)					
Yes	1 (3.2%)	0	0	0	0
No	1 (0.7%)	1 (1.6%)	0	0	1 (0.4%)
Benign prostatic hyperplasia (良性前立腺肥大症)					
Yes	0	0	0	0	0
No	1 (0.7%)	0	0	0	0
Dysmenorrhoea (月経困難症)					
Yes	1 (3.2%)	0	0	0	0
No	0	0	0	0	0
Metrorrhagia (不正子宮出血)					
Yes	0	0	0	0	0
No	0	1 (1.6%)	0	0	1 (0.4%)
Prostatitis (前立腺炎)					
Yes	0	0	0	0	0
No	1 (0.7%)	0	0	0	0
Blood and lymphatic system disorders (血液およびリンパ系障害)					
Yes	0	0	0	0	0
No	0	0	1 (0.6%)	0	1 (0.4%)
Anaemia (貧血)					
Yes	0	0	0	0	0
No	0	0	1 (0.6%)	0	1 (0.4%)
Endocrine disorders (内分泌障害)					
Yes	0	0	0	0	0
No	0	0	0	1 (1.6%)	1 (0.4%)
Thyroid cyst (甲状腺嚢腫)					
Yes	0	0	0	0	0
No	0	0	0	1 (1.6%)	1 (0.4%)
Thyroid mass (甲状腺腫瘤)					
Yes	0	0	0	0	0
No	0	0	0	1 (1.6%)	1 (0.4%)

System Organ Class Preferred Term Hepatic parameter abnormality	Placebo N = 182	Imeglimin 500 mg bid N = 75	Imeglimin 1000 mg bid N = 180	Imeglimin 1500 mg bid N = 75	Imeglimin Total N = 330
Social circumstances (社会環境)					
Yes	0	0	0	0	0
No	1 (0.7%)	0	0	0	0
Menopause (閉経)					
Yes	0	0	0	0	0
No	1 (0.7%)	0	0	0	0
Surgical and medical procedures (外科および内科処置)					
Yes	0	0	0	0	0
No	0	0	1 (0.6%)	0	1 (0.4%)
Blepharoplasty (眼瞼形成)					
Yes	0	0	0	0	0
No	0	0	1 (0.6%)	0	1 (0.4%)

- Abbreviations: bid, Twice a day; AE, Adverse event; TEAE, Treatment Emergent AE
- Hepatic parameter abnormality is defined as any one of following parameter applied: Total Bilirubin >= 1.6 mg/dL; Aspartate aminotransferase (AST) >= 1.25 x Upper Limit of Normal (ULN); AST >= 50 IU; Alanine aminotransferase (ALT) >= 1.25 x ULN; ALT >= 50 IU; Alkaline phosphatase >= 1.25 x ULN; Gamma glutamyl transferase >= 1.5 x ULN.
- All adverse events were coded using MedDRA dictionary version 20.1.
- Percentages are based on "Number of patients".

Control No:<<t-s-165-subae-24wdb.sas, 2020-03-06T00:12:48>>