Safety and Effectiveness of SB2 (Infliximab Biosimilar) in Adult Patients with Immune-Mediated Inflammatory Diseases, a Post-Marketing Surveillance in Korea

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Supplemental Materials

Supplemental Table S1: Participating study sites where the study protocol was reviewed and approved by the institutional review board (IRB)

Study site name	Approval code from IRBs (Study identification code)	Number of subjects for data collection	Number of subjects for safety assessment
Kangbuk Samsung Hospital[a]	KBSMC PMS2017-005	20	20
Inje University, Busan Paik Hospital	18-0007	84	84
Kosin University Gospel Hospital	PMS2018-020	2	2
Samsung Changwon Hospital[b]	PMS2018-002	2	1
Hallym University Chuncheon Sacred Heart Hospital	PMS2018-003	10	10
Wonkwang University Hospital	PMS2018-018	20	20
Changwon Fatima Hospital	CFH-2018-10	8	8
Samsung Changwon Hospital[c]	PMS2018-005	5	5
Keimyung University Dongsan Hospital[b]	PMS2018-057	2	2
Keimyung University Dongsan Hospital[c]	PMS2018-056	17	17
Inje University Sanggye Paik Hospital	PMS2019-001	9	9
Kyungpook National University Chilgok Hospital	PMS2019-001	2	2

[a] Study site of principle investigator

[b] Division of Gastroenterology and Hepatology, Department of Internal Medicine

[c] Division of Rheumatology, Department of Internal Medicine

Supplemental Table S2: SB2 treatment schedule for different indications [a]

Rheumatoid arthritis Initially: 3 mg/kg is infused intravenously over a 2-hour period. 3 mg/kg is administered at 2 and 6 weeks respectively after the initial administration date. Maintenance: 3 mg/kg is administered every 8 weeks. This drug is administered in combination with MTX. Based on the data available so far, it seems that the clinical response is mostly observed within 12 weeks of treatment. If a patient shows an inadequate response or loses response after this period, gradually increasing the dose stepwise by approximately 1.5 mg/kg every 8 weeks up to a maximum of 7.5 mg/kg may be considered. Alternatively, administration of 3 mg/kg every 4 weeks may be considered. If a patient shows an adequate response, the patient is treated continuously with the selected dose or dose frequency. The continuation of the therapy should be carefully reconsidered in patients who show no evidence of therapeutic benefit within the first 12 weeks of treatment or after dose adjustment.
Ankylosing spondylitis Initially: 5 mg/kg is infused intravenously for over a 2-hour period. 5 mg/kg is administered at 2 and 6 weeks respectively after the initial administration date. If a patient does not show any response until Week 6 (i.e., until after 2 doses), this drug should not be administered additionally. If a patient shows response, the drug should be administered as shown below. Maintenance: 5 mg/kg is infused intravenously every 6 to 8 weeks.
Adult Crohn's disease *Moderately to severely active Crohn's disease* Initially: 5 mg/kg is infused intravenously for at a 2-hour period, and patients who have a response within 2 weeks after the initial administration receive the next dose as shown below. Maintenance: 5 mg/kg is infused intravenously at Weeks 2 and 6 after the initial administration, and every 8 weeks thereafter. If the response decreases after responding to the initial treatment, the dose can be increased up to 10 mg/kg. There are no available data that support the treatment using this drug in patients who do not respond within 2 weeks after the initial administration. *Fistulizing, active Crohn's disease* Initially: 5 mg/kg is infused intravenously for over a 2-hour period. 5 mg/kg is administered at 2 and 6 weeks respectively after the initial administration date. If a patient does not show any response after 3 doses, this drug should not be administered additionally. If a patient shows response, the drug should be administered as shown below. Maintenance: 5 mg/kg is infused intravenously every 8 weeks. If the response decreases after responding to the initial treatment, the dose is increased up to 10 mg/kg.
Pediatric Crohn's disease (aged 6 to 17 years)

Initially: 5 mg/kg is infused intravenously over a 2-hour period. 5 mg/kg is administered at 2 and 6 weeks respectively after the initial administration date. Maintenance: 5 mg/kg is infused intravenously every 8 weeks. In some patients, the administration interval may be shortened or extended to maintain the clinical benefit. There are no data that support the continuation of treatment using this drug in pediatric patients who do not respond within 10 weeks after the initial administration. No studies on this drug have been conducted in patients with Crohn's disease who are aged younger than 6 years.
Adult ulcerative colitis
Initially: 5 mg/kg is infused intravenously over a 2-hour period. 5 mg/kg is administered at 2 and 6 weeks respectively after the initial administration date. Maintenance: 5 mg/kg is administered every 6 to 8 weeks. Based on the data available so far, it seems that the clinical response is mostly observed within 14 weeks of treatment (3 doses). The continuation of the therapy should be carefully reconsidered in patients who show no evidence of therapeutic benefit within this period.
Pediatric ulcerative colitis (aged 6 to 17 years)
Initially: 5 mg/kg is infused intravenously over a 2-hour period. 5 mg/kg is administered at 2 and 6 weeks respectively after the initial administration date. Maintenance: 5 mg/kg is infused intravenously every 8 weeks. There are no data that support the continuation of treatment using this drug in pediatric and adolescent patients who do not respond within the first 8 weeks after the initial administration. No studies on the safety and efficacy of this drug have been conducted in patients with ulcerative colitis who are aged younger than 6 years.
Psoriatic arthritis
Initially: 5 mg/kg is infused intravenously over a 2-hour period. 5 mg/kg is administered at 2 and 6 weeks respectively after the initial administration date. Maintenance: 5 mg/kg is administered every 8 weeks.
Psoriasis
Initially: 5 mg/kg is infused intravenously over a 2-hour period. 5 mg/kg is administered at 2 and 6 weeks respectively after the initial administration date. Maintenance: 5 mg/kg is administered every 8 weeks. If a patient does not show any response after 14 weeks (after 4 doses), this drug is not administered additionally.
Intestinal Behçet's Disease
Initially: 5 mg/kg is infused intravenously over a 2-hour period. 5 mg/kg is administered at 2 and 6 weeks respectively after the initial administration date. Maintenance: 5 mg/kg is administered every 8 weeks.

During the treatment using this drug, another treatment such as a corticosteroid or an immunosuppressant can be combined.

[a] Indication and treatment schedule based on SB2 Korean label

Supplemental Table S3: Incidence rate of AEs and ADRs

SOC/PT	AE		ADR		SAE		Serious ADR	
	n(%), [E]	95% CI	n(%), [E]	95% CI	n(%), [E]	95% CI	n(%), [E]	95% CI
Total	23(12.78), [38]	[8.28, 18.55]	14(7.78), [20]	[4.32, 12.71]	3(1.67), [7]	[0.35, 4.79]	1(0.56), [1]	[0.01, 3.06]
Ear and labyrinth disorders	**1(0.56), [1]**	**[0.01, 3.06]**	**0(0.00), [0]**	**[0.00, 0.00]**	**0(0.00), [0]**	**[0.00, 0.00]**	**0(0.00), [0]**	**[0.00, 0.00]**
Tinnitus	1(0.56), [1]	[0.01, 3.06]	0(0.00), [0]	[0.00, 0.00]	0(0.00), [0]	[0.00, 0.00]	0(0.00), [0]	[0.00, 0.00]
Gastrointestinal disorders	**6(3.33), [7]**	**[1.23, 7.11]**	**3(1.67), [3]**	**[0.35, 4.79]**	**2(1.11), [3]**	**[0.13, 3.96]**	**1(0.56), [1]**	**[0.01, 3.06]**
Vomiting	2(1.11), [2]	[0.13, 3.96]	1(0.56), [1]	[0.01, 3.06]	1(0.56), [1]	[0.01, 3.06]	0(0.00), [0]	[0.00, 0.00]
Abdominal pain	1(0.56), [1]	[0.01, 3.06]	1(0.56), [1]	[0.01, 3.06]	0(0.00), [0]	[0.00, 0.00]	0(0.00), [0]	[0.00, 0.00]
Anal fissure	1(0.56), [1]	[0.01, 3.06]	0(0.00), [0]	[0.00, 0.00]	0(0.00), [0]	[0.00, 0.00]	0(0.00), [0]	[0.00, 0.00]
Colitis	1(0.56), [1]	[0.01, 3.06]	1(0.56), [1]	[0.01, 3.06]	1(0.56), [1]	[0.01, 3.06]	1(0.56), [1]	[0.01, 3.06]
Duodenal ulcer	1(0.56), [1]	[0.01, 3.06]	0(0.00), [0]	[0.00, 0.00]	0(0.00), [0]	[0.00, 0.00]	0(0.00), [0]	[0.00, 0.00]
Nausea	1(0.56), [1]	[0.01, 3.06]	0(0.00), [0]	[0.00, 0.00]	1(0.56), [1]	[0.01, 3.06]	0(0.00), [0]	[0.00, 0.00]
General disorders and administration site conditions	**1(0.56), [1]**	**[0.01, 3.06]**	**1(0.56), [1]**	**[0.01, 3.06]**	**0(0.00), [0]**	**[0.00, 0.00]**	**0(0.00), [0]**	**[0.00, 0.00]**
Pain	1(0.56), [1]	[0.01, 3.06]	1(0.56), [1]	[0.01, 3.06]	0(0.00), [0]	[0.00, 0.00]	0(0.00), [0]	[0.00, 0.00]
Hepatobiliary disorders	**1(0.56), [1]**	**[0.01, 3.06]**	**0(0.00), [0]**	**[0.00, 0.00]**	**1(0.56), [1]**	**[0.01, 3.06]**	**0(0.00), [0]**	**[0.00, 0.00]**
Biliary cirrhosis	1(0.56), [1]	[0.01, 3.06]	0(0.00), [0]	[0.00, 0.00]	1(0.56), [1]	[0.01, 3.06]	0(0.00), [0]	[0.00, 0.00]
Immune system disorders	**1(0.56), [1]**	**[0.01, 3.06]**	**1(0.56), [1]**	**[0.01, 3.06]**	**0(0.00), [0]**	**[0.00, 0.00]**	**0(0.00), [0]**	**[0.00, 0.00]**
Hypersensitivity	1(0.56), [1]	[0.01, 3.06]	1(0.56), [1]	[0.01, 3.06]	0(0.00), [0]	[0.00, 0.00]	0(0.00), [0]	[0.00, 0.00]
Infections and infestations	**2(1.11), [4]**	**[0.13, 3.96]**	**0(0.00), [0]**	**[0.00, 0.00]**	**1(0.56), [2]**	**[0.01, 3.06]**	**0(0.00), [0]**	**[0.00, 0.00]**

SOC/PT	AE		ADR		SAE		Serious ADR	
	n(%), [E]	95% CI	n(%), [E]	95% CI	n(%), [E]	95% CI	n(%), [E]	95% CI
Disseminated tuberculosis	1(0.56), [1]	[0.01, 3.06]	0(0.00), [0]	[0.00, 0.00]	1(0.56), [2]	[0.01, 3.06]	0(0.00), [0]	[0.00, 0.00]
Encephalitis viral	1(0.56), [1]	[0.01, 3.06]	0(0.00), [0]	[0.00, 0.00]	1(0.56), [2]	[0.01, 3.06]	0(0.00), [0]	[0.00, 0.00]
Encephalitis	1(0.56), [1]	[0.01, 3.06]	0(0.00), [0]	[0.00, 0.00]	0(0.00), [0]	[0.00, 0.00]	0(0.00), [0]	[0.00, 0.00]
Hordeolum	1(0.56), [1]	[0.01, 3.06]	0(0.00), [0]	[0.00, 0.00]	0(0.00), [0]	[0.00, 0.00]	0(0.00), [0]	[0.00, 0.00]
Injury, poisoning and procedural complications	**1(0.56), [1]**	**[0.01, 3.06]**	**0(0.00), [0]**	**[0.00, 0.00]**	**0(0.00), [0]**	**[0.00, 0.00]**	**0(0.00), [0]**	**[0.00, 0.00]**
Hip fracture	1(0.56), [1]	[0.01, 3.06]	0(0.00), [0]	[0.00, 0.00]	0(0.00), [0]	[0.00, 0.00]	0(0.00), [0]	[0.00, 0.00]
Investigations	**1(0.56), [1]**	**[0.01, 3.06]**	**1(0.56), [1]**	**[0.01, 3.06]**	**0(0.00), [0]**	**[0.00, 0.00]**	**0(0.00), [0]**	**[0.00, 0.00]**
Aspartate aminotransferase increased	1(0.56), [1]	[0.01, 3.06]	1(0.56), [1]	[0.01, 3.06]	0(0.00), [0]	[0.00, 0.00]	0(0.00), [0]	[0.00, 0.00]
Metabolism and nutrition disorders	**1(0.56), [1]**	**[0.01, 3.06]**	**0(0.00), [0]**	**[0.00, 0.00]**	**0(0.00), [0]**	**[0.00, 0.00]**	**0(0.00), [0]**	**[0.00, 0.00]**
Decreased appetite	1(0.56), [1]	[0.01, 3.06]	0(0.00), [0]	[0.00, 0.00]	0(0.00), [0]	[0.00, 0.00]	0(0.00), [0]	[0.00, 0.00]
Musculoskeletal and connective tissue disorders	**1(0.56), [1]**	**[0.01, 3.06]**	**0(0.00), [0]**	**[0.00, 0.00]**	**0(0.00), [0]**	**[0.00, 0.00]**	**0(0.00), [0]**	**[0.00, 0.00]**
Polyarthritis	1(0.56), [1]	[0.01, 3.06]	0(0.00), [0]	[0.00, 0.00]	0(0.00), [0]	[0.00, 0.00]	0(0.00), [0]	[0.00, 0.00]
Nervous system disorders	**6(3.33), [7]**	**[1.23, 7.11]**	**5(2.78), [5]**	**[0.91, 6.36]**	**0(0.00), [0]**	**[0.00, 0.00]**	**0(0.00), [0]**	**[0.00, 0.00]**
Paraesthesia	4(2.22), [4]	[0.61, 5.59]	4(2.22), [4]	[0.61, 5.59]	0(0.00), [0]	[0.00, 0.00]	0(0.00), [0]	[0.00, 0.00]
Headache	2(1.11), [2]	[0.13, 3.96]	1(0.56), [1]	[0.01, 3.06]	0(0.00), [0]	[0.00, 0.00]	0(0.00), [0]	[0.00, 0.00]
Dizziness	1(0.56), [1]	[0.01, 3.06]	0(0.00), [0]	[0.00, 0.00]	0(0.00), [0]	[0.00, 0.00]	0(0.00), [0]	[0.00, 0.00]

SOC/PT	AE		ADR		SAE		Serious ADR	
	n(%), [E]	95% CI	n(%), [E]	95% CI	n(%), [E]	95% CI	n(%), [E]	95% CI
Psychiatric disorders	**1(0.56), [1]**	**[0.01, 3.06]**	**0(0.00), [0]**	**[0.00, 0.00]**	**0(0.00), [0]**	**[0.00, 0.00]**	**0(0.00), [0]**	**[0.00, 0.00]**
Irritability	1(0.56), [1]	[0.01, 3.06]	0(0.00), [0]	[0.00, 0.00]	0(0.00), [0]	[0.00, 0.00]	0(0.00), [0]	[0.00, 0.00]
Respiratory, thoracic and mediastinal disorders	**1(0.56), [2]**	**[0.01, 3.06]**	**0(0.00), [0]**	**[0.00, 0.00]**	**0(0.00), [0]**	**[0.00, 0.00]**	**0(0.00), [0]**	**[0.00, 0.00]**
Cough	1(0.56), [1]	[0.01, 3.06]	0(0.00), [0]	[0.00, 0.00]	0(0.00), [0]	[0.00, 0.00]	0(0.00), [0]	[0.00, 0.00]
Productive cough	1(0.56), [1]	[0.01, 3.06]	0(0.00), [0]	[0.00, 0.00]	0(0.00), [0]	[0.00, 0.00]	0(0.00), [0]	[0.00, 0.00]
Skin and subcutaneous tissue disorders	**6(3.33), [8]**	**[1.23, 7.11]**	**6(3.33), [8]**	**[1.23, 7.11]**	**0(0.00), [0]**	**[0.00, 0.00]**	**0(0.00), [0]**	**[0.00, 0.00]**
Pruritus	6(3.33), [6]	[1.23, 7.11]	6(3.33), [6]	[1.23, 7.11]	0(0.00), [0]	[0.00, 0.00]	0(0.00), [0]	[0.00, 0.00]
Rash	1(0.56), [1]	[0.01, 3.06]	1(0.56), [1]	[0.01, 3.06]	0(0.00), [0]	[0.00, 0.00]	0(0.00), [0]	[0.00, 0.00]
Urticaria	1(0.56), [1]	[0.01, 3.06]	1(0.56), [1]	[0.01, 3.06]	0(0.00), [0]	[0.00, 0.00]	0(0.00), [0]	[0.00, 0.00]
Vascular disorders	**1(0.56), [1]**	**[0.01, 3.06]**	**1(0.56), [1]**	**[0.01, 3.06]**	**0(0.00), [0]**	**[0.00, 0.00]**	**0(0.00), [0]**	**[0.00, 0.00]**
Hypertension	1(0.56), [1]	[0.01, 3.06]	1(0.56), [1]	[0.01, 3.06]	0(0.00), [0]	[0.00, 0.00]	0(0.00), [0]	[0.00, 0.00]

ADR; adverse drug reaction; AE, adverse event; CI, confidence interval; E, number of events; n, number of patients with adverse event(s); PT, Preferred Term; SAE, serious adverse event; SOC, System Organ Class.

Supplemental Table S4. Incidence rate (events/100 patient-years) of AEs and ADRs

SOC	AE		ADR		SAE		Serious ADR	
PT	E/E'	95% CI	E/E'	95% CI	E/E'	95% CI	E/E'	95% CI
Any event	38/43.01	[25.90, 64.40]	20/22.64	[10.86, 38.68]	7/7.92	[1.91, 18.13]	1/1.13	[0.00, 5.69]
Ear and labyrinth disorders	**1/1.13**	**[0.00, 5.69]**	**0/0.00**	**[0.00, 0.00]**	**0/0.00**	**[0.00, 0.00]**	**0/0.00**	**[0.00, 0.00]**
Tinnitus	1/1.13	[0.00, 5.69]	0/0.00	[0.00, 0.00]	0/0.00	[0.00, 0.00]	0/0.00	[0.00, 0.00]
Gastrointestinal disorders	**7/7.92**	**[1.91, 18.13]**	**3/3.40**	**[0.24, 10.58]**	**3/3.40**	**[0.24, 10.58]**	**1/1.13**	**[0.00, 5.69]**
Vomiting	2/2.26	[0.06, 8.35]	1/1.13	[0.00, 5.69]	1/1.13	[0.00, 5.69]	0/0.00	[0.00, 0.00]
Abdominal pain	1/1.13	[0.00, 5.69]	1/1.13	[0.00, 5.69]	0/0.00	[0.00, 0.00]	0/0.00	[0.00, 0.00]
Anal fissure	1/1.13	[0.00, 5.69]	0/0.00	[0.00, 0.00]	0/0.00	[0.00, 0.00]	0/0.00	[0.00, 0.00]
Colitis	1/1.13	[0.00, 5.69]	1/1.13	[0.00, 5.69]	1/1.13	[0.00, 5.69]	1/1.13	[0.00, 5.69]
Duodenal ulcer	1/1.13	[0.00, 5.69]	0/0.00	[0.00, 0.00]	0/0.00	[0.00, 0.00]	0/0.00	[0.00, 0.00]
Nausea	1/1.13	[0.00, 5.69]	0/0.00	[0.00, 0.00]	1/1.13	[0.00, 5.69]	0/0.00	[0.00, 0.00]
General disorders and administration site conditions	**1/1.13**	**[0.00, 5.69]**	**1/1.13**	**[0.00, 5.69]**	**0/0.00**	**[0.00, 0.00]**	**0/0.00**	**[0.00, 0.00]**
Pain	1/1.13	[0.00, 5.69]	1/1.13	[0.00, 5.69]	0/0.00	[0.00, 0.00]	0/0.00	[0.00, 0.00]
Hepatobiliary disorders	**1/1.13**	**[0.00, 5.69]**	**0/0.00**	**[0.00, 0.00]**	**1/1.13**	**[0.00, 5.69]**	**0/0.00**	**[0.00, 0.00]**
Biliary cirrhosis	1/1.13	[0.00, 5.69]	0/0.00	[0.00, 0.00]	1/1.13	[0.00, 5.69]	0/0.00	[0.00, 0.00]
Immune system disorders	**1/1.13**	**[0.00, 5.69]**	**1/1.13**	**[0.00, 5.69]**	**0/0.00**	**[0.00, 0.00]**	**0/0.00**	**[0.00, 0.00]**
Hypersensitivity	1/1.13	[0.00, 5.69]	1/1.13	[0.00, 5.69]	0/0.00	[0.00, 0.00]	0/0.00	[0.00, 0.00]

SOC	AE		ADR		SAE		Serious ADR	
PT	E/E'	95% CI	E/E'	95% CI	E/E'	95% CI	E/E'	95% CI
Infections and infestations	**4/4.53**	**[0.55, 12.61]**	**0/0.00**	**[0.00, 0.00]**	**2/2.26**	**[0.06, 8.35]**	**0/0.00**	**[0.00, 0.00]**
Disseminated tuberculosis	1/1.13	[0.00, 5.69]	0/0.00	[0.00, 0.00]	1/1.13	[0.00, 5.69]	0/0.00	[0.00, 0.00]
Encephalitis	1/1.13	[0.00, 5.69]	0/0.00	[0.00, 0.00]	0/0.00	[0.00, 0.00]	0/0.00	[0.00, 0.00]
Encephalitis viral	1/1.13	[0.00, 5.69]	0/0.00	[0.00, 0.00]	1/1.13	[0.00, 5.69]	0/0.00	[0.00, 0.00]
Hordeolum	1/1.13	[0.00, 5.69]	0/0.00	[0.00, 0.00]	0/0.00	[0.00, 0.00]	0/0.00	[0.00, 0.00]
Injury, poisoning and procedural complications	**1/1.13**	**[0.00, 5.69]**	**0/0.00**	**[0.00, 0.00]**	**0/0.00**	**[0.00, 0.00]**	**0/0.00**	**[0.00, 0.00]**
Hip fracture	1/1.13	[0.00, 5.69]	0/0.00	[0.00, 0.00]	0/0.00	[0.00, 0.00]	0/0.00	[0.00, 0.00]
Investigations	**1/1.13**	**[0.00, 5.69]**	**1/1.13**	**[0.00, 5.69]**	**0/0.00**	**[0.00, 0.00]**	**0/0.00**	**[0.00, 0.00]**
Aspartate aminotransferase increased	1/1.13	[0.00, 5.69]	1/1.13	[0.00, 5.69]	0/0.00	[0.00, 0.00]	0/0.00	[0.00, 0.00]
Metabolism and nutrition disorders	**1/1.13**	**[0.00, 5.69]**	**0/0.00**	**[0.00, 0.00]**	**0/0.00**	**[0.00, 0.00]**	**0/0.00**	**[0.00, 0.00]**
Decreased appetite	1/1.13	[0.00, 5.69]	0/0.00	[0.00, 0.00]	0/0.00	[0.00, 0.00]	0/0.00	[0.00, 0.00]
Musculoskeletal and connective tissue disorders	**1/1.13**	**[0.00, 5.69]**	**0/0.00**	**[0.00, 0.00]**	**0/0.00**	**[0.00, 0.00]**	**0/0.00**	**[0.00, 0.00]**
Polyarthritis	1/1.13	[0.00, 5.69]	0/0.00	[0.00, 0.00]	0/0.00	[0.00, 0.00]	0/0.00	[0.00, 0.00]
Nervous system disorders	**7/7.92**	**[1.91, 18.13]**	**5/5.66**	**[0.94, 14.53]**	**1/1.13**	**[0.00, 5.69]**	**0/0.00**	**[0.00, 0.00]**

SOC	AE		ADR		SAE		Serious ADR	
PT	**E/E'**	**95% CI**	**E/E'**	**95% CI**	**E/E'**	**95% CI**	**E/E'**	**95% CI**
Paraesthesia	4/4.53	[0.55, 12.61]	4/4.53	[0.55, 12.61]	0/0.00	[0.00, 0.00]	0/0.00	[0.00, 0.00]
Headache	2/2.26	[0.06, 8.35]	1/1.13	[0.00, 5.69]	0/0.00	[0.00, 0.00]	0/0.00	[0.00, 0.00]
Dizziness	1/1.13	[0.00, 5.69]	0/0.00	[0.00, 0.00]	1/1.13	[0.00, 5.69]	0/0.00	[0.00, 0.00]
Psychiatric disorders	**1/1.13**	**[0.00, 5.69]**	**0/0.00**	**[0.00, 0.00]**	**0/0.00**	**[0.00, 0.00]**	**0/0.00**	**[0.00, 0.00]**
Irritability	1/1.13	[0.00, 5.69]	0/0.00	[0.00, 0.00]	0/0.00	[0.00, 0.00]	0/0.00	[0.00, 0.00]
Respiratory, thoracic and mediastinal disorders	**2/2.26**	**[0.06, 8.35]**	**0/0.00**	**[0.00, 0.00]**	**0/0.00**	**[0.00, 0.00]**	**0/0.00**	**[0.00, 0.00]**
Cough	1/1.13	[0.00, 5.69]	0/0.00	[0.00, 0.00]	0/0.00	[0.00, 0.00]	0/0.00	[0.00, 0.00]
Productive cough	1/1.13	[0.00, 5.69]	0/0.00	[0.00, 0.00]	0/0.00	[0.00, 0.00]	0/0.00	[0.00, 0.00]
Skin and subcutaneous tissue disorders	**8/9.06**	**[2.47, 19.85]**	**8/9.06**	**[2.47, 19.85]**	**0/0.00**	**[0.00, 0.00]**	**0/0.00**	**[0.00, 0.00]**
Pruritus	6/6.79	[1.40, 16.36]	6/6.79	[1.40, 16.36]	0/0.00	[0.00, 0.00]	0/0.00	[0.00, 0.00]
Rash	1/1.13	[0.00, 5.69]	1/1.13	[0.00, 5.69]	0/0.00	[0.00, 0.00]	0/0.00	[0.00, 0.00]
Urticaria	1/1.13	[0.00, 5.69]	1/1.13	[0.00, 5.69]	0/0.00	[0.00, 0.00]	0/0.00	[0.00, 0.00]
Vascular disorders	**1/1.13**	**[0.00, 5.69]**	**1/1.13**	**[0.00, 5.69]**	**0/0.00**	**[0.00, 0.00]**	**0/0.00**	**[0.00, 0.00]**
Hypertension	1/1.13	[0.00, 5.69]	1/1.13	[0.00, 5.69]	0/0.00	[0.00, 0.00]	0/0.00	[0.00, 0.00]

ADR, Adverse Drug Reaction; AE, Adverse Event; CI, Confidence Interval; E, frequency of events; E', frequency of event per 100 patient-years; PT, Preferred Term; SAE, serious adverse event; SOC, System Organ Class.