[Detailed information regarding anaphylactic shock and anaphylaxis occurred in clinical trials of Joyclu]

Case 1	Sex Age	Reported term MedDRA preferred term	Time of onset	Outcome/ Day of outcome (day)	Severity/ Seriousness	Relationship/ Measures taken	Other treatments
	Female 55	Anaphylactic Shock Anaphylactic Shock	Day 1 (day of administration)	Recovered (6 days after onset)	Moderate Serious	Discontinuation	concomitant drugs, drainage

Day	Clinical course and treatment
Day 1 (day of administration)	10:31 The investigational drug was administrated to the knee in concern (right knee). Blood pressure (BP) before administration of the investigational drug was 141/78 mmHg. After the administration, swelling and pain in her knee were noticed on her way to work. 13:00 Urticaria appeared. 15:00 Nausea accompanied. 16:23 The patient made a phone call to the investigational coordinator to tell about the symptoms above and was told to visit the hospital. 18:20 The patient reached the investigational site with the symptoms of general rash, coldness, feeling ill, facial pallor and tremor. 18:30 Infusion of saline 100 mL and dexamethasone sodium phosphate was started. Joint fluid drainage was conducted because her right knee was swelling. Blood pressure BP: 88/64 mmHg. 19:00 Infusion ended. BP: 99/72 mmHg. 19:30 Because symptoms were recovering, the patient went home. Betamethasone valerate/gentamicin sulfate and bilastine were prescribed for 5 days. Continuing the investigation was judged to be difficult, because the event occurred after administration of investigational drug and the relationship with the investigational drug could not be ruled out. General bacterial test and immunology test of the joint fluid in the knee in concern and laboratory tests were conducted.
Day 4	She had no symptoms except that urticaria repeatedly appeared and disappeared.
Day 6	The patient was reexamined. All the oral drugs prescribed at the start day of investigational drug administration had been taken and prescription was discontinued. No urticaria was observed after this day. General condition was good. (outcome: recovered)
Patient background: female, 55 years old, height: 16X.4 cm, body weight: 6X.8 kg Medical history: none, concomitant disease: back pain, osteoarthritis Concomitant drugs (drugs used before onset of adverse event): none Other adverse events: none	

Case 2	Sex Age	Reported term MedDRA preferred term	Time of onset	Outcome/ Day of outcome (day)	Severity/ Seriousness	Relationship/ Measures taken	Other treatments
	Female 52	Anaphylaxis Anaphylactic reaction	Day 1 (day of administration)	Recovered (8 days after onset)	Moderate Serious	Discontinuation	Concomitant drugs

Days after administration	Clinical course and treatment
Day 1 of administration	12:10 administration of the investigational drug, blood pressure (BP) prior to the administration: 129/85 mmHg around 12:30 The patient went back home without any adverse reaction around 14:30 Call from the patient. Swelling in the treatment site (right knee) with sensations of burning. Doctor took a wait-and-see approach. around 15:00 Onset of itching around 15:30 Call from the patient again. Generalized redness and itching. Doctor suggested to visit hospital again. around 16:00 Revisit hospital. BP: 108/74 mmHg, heart rate: 94 beats/min, SpO_2: 96%, respiratory rate: 23/min generalized rash/itching/respiratory discomfort by the move Doctor diagnosed as allergic reaction caused by the investigational drug as no concomitant drugs and the treatment was discontinued. *d*-chlorpheniramine maleate 5 mg, hydrocortisone sodium succinate 100 mg were administered by drop infusion The symptoms were in remission after the infusion. BP: 114/81 mmHg, heart rate: 75 beats/min Betamethasone/ *d*-chlorpheniramine maleate were prescribed. The patient went back home. 20:18 The patient emergently admitted to hospital as development of respiratory discomfort/ retching/ vomiting/rash. Admission to hospital after treatment. At the time of arrival, body temperature: 36.2°C, heart rate 77 beats/min, BP: 127/95 mmHg, SpO_2: 98%, respiratory rate: 28/min, respiratory discomfort (-), wheals on face and lower leg (+), itching (-), vomiting (-) lactated Ringer solution 500 mL, hydrocortisone sodium succinate 200 mg, *d*-chlorpheniramine maleate 10 mg, metoclopramide hydrochloride 10 mg were administered by drop infusion. 22:30 wheals on face and lower leg (-) Lactated Ringer solution 500 mL was administered by drop infusion
2 days after administration	Mild wheals on the both hands, thighs, lower leg, planta. Abdominal pain and diarrhea since day 1. *d*-chlorpheniramine maleate 5 mg, lactated Ringer solution 500 mL, methylprednisolone sodium succinate 500 mg, aminophylline hydrate 250 mg were administered by drop infusion. Body temperature: 37.5°C, heart rate: 85 beats/min, BP: 123/71 mmHg, respiratory rate: 14/min Rash remitted, going out from 11:00 Return to the hospital and at 20:30 wheals developed, itching hydrocortisone sodium succinate 100 mg, monoammonium glycyrrhizinate/glycine/L-cysteine hydrochloride 40 mL were administered and wheals remitted, itching disappeared
3 days after administration	Wheals developed and mild itching *d*-chlorpheniramine maleate 5 mg, hydrocortisone sodium succinate 100 mg were administered by drop infusion Wheals were at tendency to remit, go out from 8:30 20:15 Return to the hospital, bilateral cheek flushing, gradually developed generalized wheals, itching and mild pain, remitted by administration of *d*-chlorpheniramine maleate 5 mg, hydrocortisone sodium succinate 100 mg by drop infusion
4 days after administration	Wheals disappeared, itching (-), respiratory discomfort (-), claudication (-), swelling (-) Doctor decided patient discharged from hospital as the frequency of rash decreased. For in case, *d*-chlorpheniramine maleate 5 mg, hydrocortisone sodium succinate 100 mg were administered by drop infusion. Betamethasone/ *d*-chlorpheniramine maleate were increased from 3 tablets/day to 6 tablets/day and continued watch and wait.
8 days after administration	Examination for discontinuation of the treatment was conducted. After the discharge from hospital, no onset of symptoms. Betamethasone and d-chlorpheniramine maleate were terminated. (outcome: recovered)
Patient background: female, 52 years old, height: 16X.5 cm, weight: 6X.1 kg Medical history: None, Concomitant disorders : back pain Concomitant drugs (drugs used before onset of adverse event): None Other adverse reactions: diarrhea (name of symptom on the case report form: diarrhea)（1st day of administration）	

[List of anaphylactic shock and anaphylactic reaction after launch of Joyclu]

No.	Year of incidence	Age	Sex	Reported terms [preferred term]	Outcome	Time from administration to onset
1	2021	80	Female	Anaphylactic shock.	Death	Unknown (She went back home by taxi and dead near her home)
2	2021	85	Female	Cold sweat, urticarial, abdominal discomfort, decreased blood pressure	Unknown	A few minutes after administration
3	2021	Unknown	Unknown	Anaphylactic shock	Unknown	Unknown
4	2021	Unknown	Unknown	Anaphylactic reaction	Recovered	Immediately after administration
5	2021	Unknown	Unknown	Anaphylactic reaction	Unknown	Unknown (This drug was administered in forenoon, she was reexamined in the afternoon)
6	2021	83	Unknown	Anaphylactic shock	Recovering	A few minutes after administration
7	2021	81	Female	Generalized itching (itching in bilateral arm in particular), wheals	Unknown	Unknown (She visited hospital again 1 day after administration.)
8	2021	75	Female	Anaphylactic shock.	Unknown	5 to 10 minutes after administration
9	2021	70’s	Female	Anaphylactic shock	Unknown	Immediately after use
10	2021	Unknown	Unknown	Anaphylaxis, urticaria	Unknown	Unknown