SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. INITIALS	1a. COUNTRY	2. DATE OF BIRTH			2a. AGE	3. SEX	4-6. REACTION ONSET			8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION
		Day	Month	Year			Day	Month	Year	
PRIVACY	FR				76 Year(s)	M	20	Mar	2024	☐ PATIENT DIED
7+13 DESCRIBE REACTION(S) (including relevant tests/lab data) Event Verbatim [Low Level Term] IRR (fever, chills, rash) [Infusion related reaction] (10051792 v27.0) - Serious - Recovered - 20-Mar-2024/23-Mar-2024(4 Day)										☐ LIFE THREATENING ■ HOSPITALIZATION ☐ DISABILITY OR INCAPACITY ☐ CONGENITAL ANOMALY/BIRTH DEFECT ☐ OTHER MEDICALLY IMPORTANT CONDITION ☐ REQUIRED INTERVENTION (MEDICAL DEVICE)

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)		20. DID REACTION ABATE AFTER STOPPING DRUG?
#1 [Suspect] ICT01 Liquid (ICT01) #2 [Suspect] PEMBROLIZUMAB Liquid (PEMBROLIZUMAB)		☐ YES ☐ NO ■ NA
15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION	
#1 200 milligram every 3 week(s)	#1 Intravenous use	
#2 200 milligram every 3 week(s) Every 3 weeks	#2 Intravenous use	
17. INDICATION(S) FOR USE		21. DID REACTION REAPPEAR AFTER REINTRODUCTION ?
#1 Bladder [Bladder carcinoma] (10005014 v26.1) #2 Bladder [Bladder carcinoma] (10005014 v26.1)		☐ YES ☐ NO ■ NA
18. THERAPY DATES (from/to)	19. THERAPY DURATION	
#1 20-Mar-2024	#1	
#2 20-Mar-2024	#2	

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUGS(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)

23. OTHER RELEVANT HISTORY (e.g. diagnostics, allergics, pregnancy with last month of period, etc.)

From / To Dates	Description
# 1 13-Nov-2020 / ongoing	Bladder solid tumor[Bladder carcinoma] (10005014 v26.1) - continue : Yes
# 2 01-Mar-2024 / ongoing	tumoral pain[Tumor pain] (10045158 v27.0) - continue : Yes
CTCAE grade 2	

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER		26. REMARKS
Imcheck Therapeutics 31 Chemin Joseph Aiguier 13009 Marseille FR		Last receipt date : 03-Jul-2024 Study registration number : 2019-003847-31(EU)
Study no : ICT01-101 Arm no : ICT01+pembrolizumab Patient no : 01-01-089 / Center no : 01-01	24b. MFR CONTROL NO. 2024000029	25b. NAME AND ADDRESS OF REPORTER Dr. Stéphane CHAMPIAT Institut Gustave Roussy 114 Rue Edouart Vaillant 94805 Villejuif , FR
24c. DATE RECEIVED BY MANUFACTURER 22-Mar-2024	24d. REPORT SOURCE ■ STUDY ☐ LITERATURE ☐ AUTHORITY ■ HEALTH PROFESSIONAL ☐ OTHER	
DATE OF THIS REPORT 23-Aug-2024	25a. REPORT TYPE ☐ INITIAL ■ FOLLOW UP : 1	

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

Case description : Study title: A first-in-human, two-part, open-label, clinical study to assess the safety, tolerability and activity of intravenous doses of ICT01 as monotherapy and in combination with an immune checkpoint inhibitor, in patients with advanced-stage, relapsed/refractory cancer (EVICTION Study).
Initial case report received on 22-Mar-2024 from site#01-01.
This event concerns patient ID#01-01-089.

The case concerns a 76-year-old male patient with a medical history of bladder solid tumor since 13-Nov-2020.

No further medical history has been reported, neither if the patient has been managed with previous cancer treatment.

The patient was enrolled in EVICTION study, informed consent signed on 21-Feb-2024 and assigned to Part 2 – Cohort Expansion (part 1 – dose evaluation), Group H: ICT01 + pembrolizumab (200 mg Q3W).

On 20-Mar-2024, patient received the first cycle of ICT01 200mg and pembrolizumab 200mg administered via intravenous route (C1D1). Then, the patient had persistent fever grade 2 [site queried to provide a final diagnosis related to the fever as adverse event]. Due to the persistent fever, patient's hospitalization was prolonged until 21-Mar-2024. Discharge information was not provided. On the same date, patient has been managed with:

- Tazocillin (piperacillin/tazobactam) 4g, via intravenous route, every 6h
- Methylprednisolone 50mg, via intravenous route, once a day
Until the 23-Mar-2024.

Both treatments were ongoing at the moment of this report and the outcome of the event was reported as "resolving".

The last dose of ICT01 and pembrolizumab prior to the occurrence of the event were the dose in the C1D0 (20-Mar-2024).

No action was taken regarding the therapy with ICT01+pembrolizumab (dose not changed).

No concomitant medication was provided at the time of this report.

Follow-up information received on 03-Jul-2024:
The event term was specified as "IRR" (Infusion related reaction), instead of "fever" [as they are divergence between SAE form and eCRF, query was raised].
Some medical history was added : Tumoral pain (starting from 01-Mar-2024), alkaline phosphatase (starting from 19-Mar-2024) and arterial hypertension (starting in 2024).
The site provided additional information about the event : the 20-Mar-2024, the body temperature of the patient was 39°C (grade 1 fever), associated with transient confusion, that conducted to a CT Scan (normal result). The hospitalization was extended until 23-Mar-2024 [since they are discrepancy between the eCRF and SAE form, query was raised] due to the persistent fever (grade 2), with inflammatory syndrom and bicytopenia with a non-heamolytic argenerative anemia with blood count at 9 g/dl, platelets at 108 G/L and additional test was done, with PCT at 80µg/L, leucocyte count at 13.5 G/L and CRP at 120mg/L.

The 21-Mar-2024 (day 2), the patient experienced a treatment related macular rash (grade 1) that appeared on the folds (armpits), ribs and back. Renal failure was diagnosed (grade 1) with thrombocytopenia (grade 1).
The patient was managed with additional treatment: NaCl at 1.5L IV/24h, from the 21-Mar-2024 to the 23-Mar-2024.

The patient recovered the event the 23-Mar-2024 [as they are divergence between eCRF and SAE form, query raised].

REPORTER'S COMMENT :

Investigator's opinion of severity of SAE: Grade 2 - Moderate
Reported criterion for seriousness: "Hospitalisation or prolongation of existing Hospitalisation"
The investigator's opinion of relationship of "Infusion related reaction" to ICT01 was "related" and to PEMBROLIZUMAB was "unlikely" related.
The investigator considered the event unrelated to any study procedure.

SENDER'S COMMENT :

"Infusion related reaction" is expected according to the current version of the ICT01 investigator's brochure.
"Infusion related reaction" is expected according to the current version of the PEMBROLIZUMAB SmPC.

"Infusion related reaction" occurred at the same date of the first administration of ICT01 and pembrolizumab. The chronology between the onset of event and ICT01/pembrolizumab administration is compatible. "Infusion related reaction" has been observed after the administration of ICT01 in monotherapy and also in combination with pembrolizumab, according to the most recent version of approved IB. In this context, the sponsor endorses the investigator's opinion that this event of "Infusion related reaction" is probably related to ICT01, and "unlikely" related to pembrolizumab.

Analysis of similar events:
Cumulatively, at the time of this reaction, this is the 29th case of "infusion related reaction" reported as SAE/AESI since start of ICT01 development. Among these cases, 3 (11%) were grade 1, 17 (60%) were grade 2 and 8 (29%) were grade 3. All cases were resolved/recovered, and only one recovered with sequelae.

"Infusion related reaction" is listed in the current version of ICT01 IB. Risk characterization is ongoing.

13. Relevant Tests (date/test/results/units/normal low range/normal high range)

Test date	Test Name	Test results (Code / Numeric Unit / Unstructured)	Low / high
#1 : 20-Mar-2024	body temperature [Body temperature] (10005906 v27.0)	39 degree Celsius	/

Test date	Test Name	Test results (Code / Numeric Unit / Unstructured)	Low / high
#2 : 20-Mar-2024	CT Scan [CT scan] (10011603 v27.0)	Normal	/
#3 : 23-Mar-2024	CRP [C-reactive protein] (10006824 v27.0)	120 milligram per litre	/
#4 : 23-Mar-2024	leucocyte [Leukocyte count] (10080703 v27.0)	13.5 billion per litre	/
#5 : 23-Mar-2024	platelets [Platelet count] (10035525 v27.0)	108 billion per litre	/
#6 : 23-Mar-2024	PCT [Procalcitonin] (10064051 v27.0)	80 microgram per litre	/
#7 : 23-Mar-2024	blood count [Red blood cell count] (10038150 v27.0)	9 gram per decilitre	/

14-19. Drugs

#	Name	Dosage Information	Lot/Batch	Route of Admin.	Indication	Therapy dates	Therapy duration
1	[Suspect] ICT01 Liquid (ICT01)	200 milligram every 3 week(s)	UNK	Intravenous use	Bladder [Bladder carcinoma] (10005014 v26.1)	20-Mar-2024	
2	[Suspect] PEMBROLIZUMAB Liquid (PEMBROLIZUMAB)	200 milligram every 3 week(s) Every 3 weeks	UNK	Intravenous use	Bladder [Bladder carcinoma] (10005014 v26.1)	20-Mar-2024	

23. OTHER RELEVANT HISTORY continued

3 19-Mar-2024 / ongoing — Increased alkaline phosphatase[Alkaline phosphatase increased] (10001675 v27.0) - continue : Yes

CTCAE grade 1

4 uu-Uuu-2024 / ongoing — Arterial hypertension[Arterial hypertension] (10081425 v27.0) - continue : Yes