PATROL (ColoAd1-9001)

CLINICAL STUDY RESULTS SUMMARY

Study title	A multicentre observational study for the long term follow up of subjects that have been treated with enadenotucirev during interventional clinical trials (PATROL)
Brief title	Long term follow up of subjects treated with enadenotucirev
Study number	ColoAd1-9001
Study initiation date	03 July 2017 (First Patient First Visit)
Early study termination date	25 November 2020 (End of Study Notification) The analyses presented in this report are based on a database lock date of 28 November 2019 (no additional data were collected between database lock and the End of Study Notification)
Regulatory agency identifier number	EudraCT Number: 2016-004777-40
This study was conducted in compliance with International Council for Harmonisation (ICH) Good Clinical Practice (GCP), including the archiving of essential documents.	

1. PATROL study design and summary

PATROL (ColoAd1-9001) was a non-interventional, multicentre, prospective, non-randomized study designed to observe the long-term well-being and survival of subjects with advanced epithelial cancers who had been treated with enadenotucirev during interventional clinical studies; no treatment was administered as part of this observational study.

Subjects who had received enadenotucirev during a previous phase 1 clinical study were eligible for inclusion in this study.

The overall wellbeing of subjects was to be ascertained using the Eastern Cooperative Oncology Group (ECOG) performance score and any treatment for the subject's cancer was to be recorded. Follow-up of each subject was to continue until the subject's death or the end of the study, whichever came first. If the subject was deceased at study start, then just the date of death was taken from the local death register or other appropriate source from the public domain.

As there was no study treatment under investigation in this study, no pro-active safety data collection took place.

A total of 11 subjects were included in the study, only one of whom was alive at the time of study start. This subject attended the first baseline visit, at which they had the study explained to them and ECOG performance score and all cancer treatments received after enadenotucirev was discontinued were recorded. Once the subject had provided written informed consent, they were allocated a unique subject identification number. The subject died following the first post-baseline visit.

This study was terminated early following a business decision to refocus the clinical development programme on transgene-modified variants of enadenotucirev. Additionally, after further conduct of enadenotucirev interventional studies it became apparent that few patients recruited in these advanced cancer populations remained alive at the date of last follow-up, meaning that an additional long-term survival study would provide very limited additional data. Similarly, further clinical experience acquired since the design of the PATROL study demonstrated that enadenotucirev was well-tolerated with manageable and identifiable risks; therefore, additional follow-up of a very limited number of patients for long-term survival and well-being was not considered necessary.

2. Study subjects

2.1 Disposition of subjects

At the time of the premature termination of this study, 11 subjects at three participating centres in Belgium and Spain had been included in this study. Of these 11 subjects:

- Ten subjects had died before study initiation (dates of death ranged from 02 February 2015 to 27 February 2017)
- One subject signed the informed consent form and died on 24 October 2017

2.2 Demographics and other baseline characteristics

All subjects had previously been treated with enadenotucirev in the ColoAd1-1001 phase 1 study (EVOLVE; NCT02028442). One subject had been enrolled in the dose escalation stage (phase 1a) of the EVOLVE study and had a solid tumour of epithelial origin not responding to standard therapy or for which no standard treatment existed. All other patients had been enrolled in phase 1b of the EVOLVE study and had advanced or metastatic colorectal or urothelial cancer that had been treated with multiple prior lines of therapy and was not responding to standard therapy. The first doses of enadenotucirev received in prior studies were given between 11 March 2013 and 25 January 2016.

Nine out of the 11 subjects were male and the median year of birth was 1955, with an approximate median age at the time of the first dose of enadenotucirev of 60 years. Baseline demographics are shown below in Table 1. Baseline characteristics.

Table 1. Baseline characteristics

Protocol ColoAd1-9001 (PSI2)
16.4 Individual Subject Data Listings
16.4.1 Baseline Visit (Part 1 of 2)

Date of baseline visit	Date of informed consent	IC1	IC2	IC3	Year of birth	Gender	ECOG		Study number patient took part in (if other, specify)
							Not done	Grade	
		Yes	No	No	1961	Male		5	ColoAd1-1001 phase 1B
		Yes	No	No	1953	Male		5	ColoAd1-1001 phase 1B
		Yes	No	No	1971	Male		5	ColoAd1-1001 phase 1B
		Yes	No	No	1941	Male		5	ColoAd1-1001 phase 1B
		Yes	No	No	1954	Male		5	ColoAd1-1001 phase 1B
		Yes	No	No	1955	Male		5	ColoAd1-1001 phase 1B
		Yes	No	No	1973	Female		5	ColoAd1-1001 phase 1B
03/07/2017	03/07/2017	Yes	Yes	Yes	1966	Female		3	ColoAd1-1001 phase 1A
		Yes	No	No	1955	Male		5	ColoAd1-1001 phase 1B
		Yes	No	No	1949	Male		5	ColoAd1-1001 phase 1B
		Yes	No	No	1971	Male		5	ColoAd1-1001 phase 1B

IC1 = Patient has participated in a clinical trial during which they received enadenotucirev, irrespective of the route of administration, dose received or tumour type being treated.
IC2 = Patient is able and willing to provide signed and dated written informed consent.
IC3 = Patient is able to comply with study procedures in the Investigator's opinion.

2.3 Previous enadenotucirev therapy prior to entering PATROL

Prior treatment with enadenotucirev before enrollment in PATROL is summarized in Table 2. Prior enadenotucirev treatment.

Table 2. Prior enadenotucirev treatment

Protocol ColoAd1-9001 (PSI2)
16.4 Individual Subject Data Listings
16.4.1 Baseline Visit (Part 2 of 2)

Date of first dose enadenotucirev	Date of last dose enadenotucirev	Route of administration (if other, specify)	Dose schedule	Initial dose level (if other, specify)	Subsequent dose levels	Reason for discontinuing enadenotucirev	Any cancer treatments since end of study
03/11/2014	01/12/2014	IV	Multiple cycles: Weekly	6 x 10**12 vp	NK	NK	
24/11/2014	23/02/2015	IV	Multiple cycles: Weekly	6 x 10**12 vp	NK	NK	Unknown
16/02/2015	08/06/2015	IV	Multiple cycles: Weekly	3 x 10**12 vp	NK	PROGRESSIVE DISEASE	
03/11/2014	22/12/2014	IV	Multiple cycles: 3 weekly	6 x 10**12 vp	01/12/2014 -> 1X10**12	INCREASED GOT GPT	Unknown
17/11/2014	02/01/2015	IV	Multiple cycles: 3 weekly	6 x 10**12 vp	NK	PROGRESSIVE DISEASE	Unknown
24/11/2014	26/11/2014	IV	Multiple cycles: 3 weekly	6 x 10**12 vp	MISSING	PROGRESSIVE DISEASE	
02/03/2015	13/04/2015	IV	Multiple cycles: 3 weekly	3 x 10**12 vp	MISSING	PROGRESSIVE DISEASE	Unknown
11/03/2013	11/03/2013	IV	One cycle	Other: 1X10**13	NA	ACUTE LUNG INJURY	Yes
30/03/2015	26/05/2015	IV	Multiple cycles: Weekly	3 x 10**12 vp	NA	PROGRESSIVE DISEASE	
25/01/2016	29/03/2016	IV	Multiple cycles: Weekly	3 x 10**12 vp	NA	PROGRESSIVE DISEASE	
18/11/2013	31/01/2014	IV	Multiple cycles: 3 weekly	6 x 10**12 vp	NOT KNOWN	END OF TREATMENT (4 CYCLES)	Yes

3. Evaluation of response to enadenotucirev

Given the low numbers of subjects included in this study, formal data analysis was not possible or conducted.

As there was no study treatment under investigation in this study, no pro-active safety data collection took place for this study

3.1 Primary endpoint - time to death

The time to death of subjects from receiving the first dose of enadenotucirev in a clinical study is provided in Table 3. The mean survival was 450.7 days (standard deviation: 533.2 days) and median survival was 180 days.

Table 3. Time to death (all subjects)

Subject number	Survival (days)
3200-1101	92
3200-1102	159
3200-1103	737
3200-1201	180
3200-1202	167
3200-1203	230
3200-1204	104
3201-0001	1689
3201-0002	137
3201-0003	265
3400-1003	1198
Mean (standard deviation)	450.7 (533.2)
Median	180

3.2 Secondary endpoints

3.2.1 Worsening in ECOG performance score over time

The long-term well-being of the one subject who was alive at study initiation, as measured by ECOG, remained constant (at Grade 3) from the baseline to the final visit.

3.2.2 Cancer treatments administered since end of the study

Cancer treatments administered since the end of the previous enadenotucirev study were available for 2 of the 11 subjects. One subject received chemotherapy with bleomycin, cisplatin, and sorafenib and radiotherapy to the right rib cage and one subject received unspecified chemotherapy and radiotherapy.