Unique SAE Case Number: VLNC-Study-001-023-01

Primary Reporter Country: USA
Site Number: 001
Subject Number: 023

Initial report (received on 18-Sep-2018):

Serious Adverse Event: Subarachnoid hemorrhage

Coded Term: **Subarachnoid hemorrhage** (10042320) [MedDRA v. 21.1]

Relationship to Study Product: was not provided at the time of initial report

A 51 year-old female White/Caucasian subject 001-023 was enrolled in a Longitudinal Ambulatory Study to Assess Changes in Cigarette Consumption Behavior and Biomarkers of Exposure during a 6-Week Switch to Very Low Nicotine Cigarettes.

On (b) (6) 1 day after the last use of study product, the subject 001-023 was admitted to the hospital due to **subarachnoid hemorrhage.** The son stated that she underwent medical procedures to drain the blood in her brain. The recovery time was estimated at least 10 days according to the physician. Celerion was notified of this SAE on 17-Sep-2018.

The subject first received the study product Non-mentholated VLN cigarettes on 02-Aug-2018. The last use of the study product prior to the onset of this event was on 14-Sep-2018.

The onset date of event was on (b) (6) the day when the patient was admitted to hospital.

The severity of the SAE was assessed as **severe.**

The SAE outcome was not provided at the time of the initial report. Hospitalization, life-threatening and important medically event were provided as seriousness criteria.

The action taken with study product was not provided at the time of the initial report.

The action taken to treat the SAE was reported as unknown.

At the time of the initial report no information was provided regarding relevant concomitant medications taken at the time of the event and relevant medical history.

Follow-up information (received on 21-Sep-2018):

Relationship to Study Product: **unlikely related**

Follow-up information (received on 10-Oct-2018):

The SAE term was changed:
Serious Adverse Event: Intra cranial aneurysm

Coded Term: **Intracranial aneurysm** (10022758) [MedDRA v. 21.1]

The subject returned on 10-Oct-2018 to sign medical release from medical doctor discussed events leading up to the SAE. The subject reported sudden onset of unconsciousness on (b) (6) Upon regaining consciousness, she noticed she had vomited and a severe headache. She was evaluated at the hospital but then transported via ambulance to a larger intensive care unit hospital and was surgically treated for an intracranial aneurysm.

Important medical event was deleted as seriousness criterion.

The SAE outcome was updated to **resolved.**

Non-mentholated VLN cigarettes were **withdrawn** as action taken with study product.

Follow-up information (received on 18-Oct-2018):

This follow-up #3 SAE report form was sent in order to clarify previous answer in prior SAE report form submissions. The SAE was marked "resolved" with no stop date on page 2 of the previous and current SAE report form. The subject returned on 10-Oct-2018 and appeared in good health. However, the site did not know the exact stop date of SAE because the site was awaiting medical records. In section "Seriousness criteria" the site ticked "yes" and listed all that applied. The "Action taken with study product" was changed to "unchanged". The subject used no longer VLN cigarettes at the time of SAE. "Surgically treated aneurysm" was added as "Action taken to treat SAE". At the moment, the site was not aware of any medical history, signs and symptoms, diagnosis, clinical course, treatment or concomitant medications.

The action taken with study product was changed to **unchanged**.

Non-drug therapy was started as action to treat SAE and surgically treated aneurysm was specified as other action taken to treat SAE.

Follow-up information (received on 16-Nov-2018):

The SAE term was changed:
Serious Adverse Event: Sub arachnoid hemorrhage

Coded Term: **Subarachnoid hemorrhage (10042320)** [MedDRA v. 21.1]

The subject presented to emergency room (ER) with a history of severe headaches, syncopal episode, nausea and vomiting on (b) (6) A computertomography (CT) scan showed large subarachnoid hemorrhage and a CT angiogram showed an aneurysm of the right internal carotid artery. An external ventricular drain (EVD) was placed and the subject underwent coil embolization of a right supraclinoid internal cerebral artery aneurysm. The symptoms improved and the EVD was weaned. The subject was discharged home on 02-Oct-2018 and remained symptom free. The following medications were administered: acetaminophen orally 500 mg every six hours, docusate sodium orally 100 mg daily, gabapentin orally 100 mg twice daily, n. modipine orally 30 mg twice daily every four hours, ondansetron orally 4 mg (1-2 tablets) every 6 hours and oxycodon orally 5 mg (1-2 tablets) every 4 hours. The SAE was assessed as unrelated since the event of subarachnoid hemorrhage was due to a rupture of right internal cerebral artery aneurysm.

The SAE outcome was resolved on 02-Oct-2018, the day when the patient was discharged from hospital.

The seriousness criterion Life-threatening was removed.

Relationship to Study Product: **unrelated**.

Diagnostic tests specified as CT scan and CT angiogram were performed as action taken to treat SAE. Coil embolization right supraclinoid internal cerebral artery aneurysm was added as another action taken to treat the SAE.

Approval for SAE Closure:

With the signature below the case is considered closed.

11/20/18
Date

(b) (6)