

Sponsor: Sanofi Drug substance: HSV2	Study Identifiers: U1111-1183-6522; BB-IND: 18918; NCT04222985 Study code: HSV15
Title of the study: Safety and Efficacy of 4 Investigational HSV-2 Vaccines Administered by Intramuscular Route in Adults with Recurrent Genital Herpes Caused by HSV-2	
Study centers: This study was planned to be conducted at 11 centers in the United States, of which 3 enrolled participants.	
Study period: Date first participant enrolled: 18/Feb/2020 Date last participant completed: 19/May/2021 Study Status: Terminated. Sanofi decided to terminate the HSV0148 project and consequently the current study was stopped. As part of this termination decision, all clinical sites participating in the Part A of this study informed the participants about the decision assuring a 6-month safety follow-up to all participants. No safety concerns were raised during Part A of the study.	
Phase of development: I / IIa	
Objectives: All the objectives and endpoints of the study are presented below. Part A is Phase I only and Part B is Phase II only. Part B/Phase II was never conducted due to early termination of the study. As Part B was not conducted, only the objectives and endpoints related to safety (Part A) were evaluated. Primary Objectives <u>Safety</u> To describe the safety profile of the different investigational vaccine regimens. <u>Efficacy</u> For participants in Part B (not conducted), to evaluate the efficacy of each of the investigational vaccine regimens with respect to: <ul style="list-style-type: none"> ● The frequency of HSV DNA detection in the genital area (shedding rate) following a 2 dose vaccine schedule ● The proportion of participants free of recurrence at 6 months after the 2-dose vaccine schedule Secondary Objectives <u>Efficacy</u> For participants in Part B (not conducted): <ul style="list-style-type: none"> ● To describe the impact of each of the investigational vaccine regimens in terms of total number of days with genital lesion up to 6 months after Vaccination 2 (Vac 2) and number of recurrences 60 days after the second vaccination compared with the placebo group ● To describe the efficacy of each of the investigational vaccine regimens with respect to the frequency of HSV DNA detection in the genital area (shedding rate) 60 days following the first vaccination visit plus 60 days following the second vaccination visit compared with the placebo group ● To describe the efficacy of each of the investigational vaccine regimens with respect to the frequency of HSV DNA detection in the genital area (shedding rate) 60 days following the first vaccination visit compared with the placebo group <u>Immunogenicity</u> <ul style="list-style-type: none"> ● To describe the immunogenicity of each of the investigational vaccines before and after vaccination 	

Methodology:

HSV15 was a Phase I / IIa, randomized, modified double-blind, placebo-controlled, staged, multi-center trial evaluating the safety, immunogenicity, and efficacy of G103, Modified G103, HSV529, adjuvanted HSV529 (with GLA-SE), and combined G103 and HSV529 investigational vaccines in healthy adult participants, aged 18 to 55 years, with recurrent genital herpes simplex virus type 2 (HSV-2), in the US.

Prior to enrollment, and after signing the informed consent form, participants underwent a Screening Visit (V0) and provided a blood sample for confirmation of HSV-2 serostatus, and evaluation of eligibility for enrollment in the study which included a physical evaluation and biological safety test results. Concomitant medications were collected starting at V0 (28 days before Vac 1).

Multiple formulations of G103 vaccine, Modified G103 vaccine, HSV529 and G103 given concomitantly, and the sequential administration of adjuvanted HSV529 (with GLA-SE) followed by G103 were evaluated in this study.

This study was designed to include 2 parts: Part A and Part B. Part A was a safety lead-in phase for Part B. Part A was designed to assess the safety, tolerability, and immunogenicity of G103 when administered alone and in combination with HSV529 and GLA-SE in adults aged 18 to 55 years. Part B, which was not conducted due to study termination, was designed to be a 2-stage group-sequential design including a futility analysis at the end of Stage 1 to evaluate the relative reduction in shedding and the proportion of participants free of recurrence at 6 months following the second vaccination for each of the investigational vaccine regimens. It was planned that the formulations in the groups that would reach the predefined statistical threshold for the shedding and recurrence endpoints, and also would be shown to be safe in accordance with the Early Safety Data Reviews (ESDRs), would progress to Part B Stage 2. Details about Part B methodology are provided in the protocol (Appendix 1) but are not described in the current synoptic CSR because Part B was not conducted. Data are provided for Part A.

For Part A, a total of 24 participants were planned to be randomized to the following 6 groups (5 active; 1 placebo). The randomization ratio was 1:1:1:1:1:1. No more than 2 participants were to be enrolled per day; several ESDRs were to be performed, approximately every 4 weeks, based on the available data to determine if the enrollment could safely proceed and also to determine if the participant could receive the second vaccination. In addition, 2 safety data reviews were to be performed, the first after Vac 1 was completed and the second after Vac 2 was completed.

Table S1 Vaccination schedule by group: Part A

Group n=4	Product Administered Month (M) 0	Product Administered M 2
1	G103 15/15/15-2.5*†	G103 15/15/15-2.5*†
2	G103 30/30/30-2.5*‡	G103 30/30/30-2.5*‡
3	G103 30/30/30-5.0*§	G103 30/30/30-5.0*§
4	HSV529 + 5.0 µg GLA-SE (2% oil)*	G103 30/30/30-5.0*
5	HSV529 (in 1 arm) and G103 30/30/30-5.0 (in the opposite arm)	HSV529 (in 1 arm) and G103 30/30/30-5.0 (in the opposite arm)
6	Sodium Chloride 0.9% (both arms)	Sodium Chloride 0.9% (both arms)

Abbreviations: µg, micrograms; gD2, herpes simplex virus-2 glycoprotein D; GLA-SE, glucopyranosyl lipid adjuvant-stable emulsion; ud, upper domain; UL19 and UL25, structural herpes simplex virus proteins

*Administered concomitantly with 0.9% sodium chloride in the opposite arm.

†G103 (45 µg] total protein 15 µg of each UL19ud, UL25, gD2 + 2.5 µg GLA-SE [2% oil])

‡G103 (90 µg total protein 30 µg of each UL19ud, UL25, gD2 + 2.5 µg GLA-SE [2% oil])

§G103 (90 µg total protein 30 µg of each UL19ud, UL25, gD2 + 5.0 µg GLA-SE [2% oil])

Participants in Group 5 received HSV529 vaccine in 1 arm and G103 30/30/30-5 in the opposite arm at Month (M) 0 (Visit [V] 01) and M 2 (V05). Therefore, in order to maintain the study-blind, participants in Groups 1 through 4 received an investigational vaccine in 1 arm and an injection of 0.9% sodium chloride in the opposite arm at M 0 (V01) and M 2 (V05). Participants in Group 6 received 2 injections of 0.9% sodium chloride (1 injection in each arm) at M 0 (V01) and M 2 (V05). Given that different study products were administered in each group and each participant was randomly assigned to receive 1 injection per arm, 1 or 2 unblinded persons at the study site were to be used at each study site for both Part A and Part B (Part B was not conducted due to study termination) to prepare and administer the vaccine (depending on the staff assignments at the study site, this could either be the same unblinded person or 2 unblinded persons). The vaccine-preparing person and/or the administrator were not involved in any of the blinded study assessments (eg, safety). Taking into account the fact that the volumes to be injected were different (0.25 mL only for HSV529 and 0.5 mL for all other Investigational Products), the syringes were masked (ie, covered with dark plastic) to keep the blind of the participants and other members of the clinical site.

Collection of safety data

Participants in Part A were to collect safety data in the DCs/eDCs and concomitant medications, including HSV daily symptoms and HSV suppressive therapy from V0 to V09.

Blood sampling

For Part A, all participants were to provide blood samples at V0 (screening/baseline), V01 (collect blood sample before vaccination), V02, V03, V04, V05 (collect blood sample before vaccination), V06, V07, and V09.

Early safety data review

Periodical blinded ESDRs were conducted approximately every 4 weeks on all the available data to evaluate the enrolled participants who received any vaccination and provided safety data for the 7 days post-vaccination (after any dose); this was to determine if the participants could continue with the second vaccination and to determine if the enrollment in the study could safely be continued.

If any safety signal was detected during ESDRs after the first vaccination or after the second vaccination, or at any time during Part A, including any related SAEs, adverse events of special interest (AESIs), or potentially immune-mediated medical conditions (pIMMCs) that under the judgement of the Investigator could represent a safety concern, the affected participant(s) could not receive any further vaccination and was/were to be followed for safety monitoring.

Also, if any biological safety test result abnormalities of a moderate and/or severe designation were detected or if mild abnormalities that under the judgement of the Investigator could be considered as a safety concern, the affected participants could not receive any further vaccination and were followed for safety monitoring.

Additional teams and boards were also involved in the monitoring of the study.

Safety halting rules for Part A included, at any moment or as a result of the ESDRs:

- Any related SAEs assessed by the Principal Investigator or the Sponsor
- > 15% of participants with Grade 3 solicited reactions/unsolicited AEs of a similar nature independently of the duration based on the entire cohort of Part A (24 participants)

<p>Number of participants:</p> <p style="padding-left: 40px;">Planned: 24 (Part A); 196 (Part B Stage 1); 161 (Part B Stage 2)</p> <p style="padding-left: 40px;">Randomized: 24</p> <p style="padding-left: 40px;">Vaccinated: 24</p> <p>Evaluated:</p> <p style="padding-left: 40px;">Safety: 24</p>
<p>Diagnosis and criteria for inclusion:</p> <p>The study included male and female participants in good general health, HSV-2 seropositive, with a history of established HSV-2 infection \geq 1 year and aged 18 to 55 years on the day of inclusion.</p>
<p>Study products:</p> <p>Investigational medicinal product 1: G103 ([HSV-2 UL19ud, UL25, and gD2] Therapeutic Vaccine/GLA-SE Adjuvant)</p> <p>Form: Liquid solution</p> <p>Route: Intramuscular (IM)</p> <p>Investigational medicinal product 2: Modified G103 ([HSV-2 UL19ud and UL25] Therapeutic Vaccine/GLA-SE Adjuvant)</p> <p>It was originally planned that an additional group of participants (Group 7) would receive investigational product 2 during Part B of the study. As this part was not conducted due to early termination of the study, investigational product 2 was not tested.</p> <p>Form: Liquid solution</p> <p>Route: IM</p> <p>Investigational medicinal product 3: HSV529 (Live, Replication-defective HSV-2 virus)</p> <p>Form: Liquid suspension</p> <p>Route: IM</p> <p>Investigational medicinal product 4: HSV529 (Live, Replication-defective HSV-2 virus) + GLA-SE Adjuvant</p> <p>Form: Liquid suspension</p> <p>Route: IM</p> <p>Control product: Normal saline (Placebo)</p> <p>Form: Liquid solution</p> <p>Route: IM</p>
<p>Duration of Study Intervention: Approximately 16 months</p>

Criteria for evaluation:

Primary Endpoints

Safety

Safety was to be described for all participants:

- Occurrence, nature (Medical Dictionary for Regulatory Activities preferred term [MedDRA PT]), duration, intensity, and relationship to vaccination of any unsolicited systemic adverse events (AEs) reported in the 4 hours after any vaccination in Part A, or reported in the 30 minutes after any vaccination in Part B.
- Occurrence, time to onset, number of days of occurrence, intensity, action taken, and whether the reaction led to early termination from the trial, of solicited (prelisted in the participant's Diary Card/electronic Diary Card (DC/eDC) and case report book (CRB) injection site reactions and systemic reactions occurring up to 7 days after vaccination.
- Occurrence, nature (MedDRA PT), time to onset, duration, intensity, relationship to vaccination (for systemic AEs only), and whether the event led to early termination from the trial, of unsolicited AEs up to 30 days after vaccination.
- Occurrence, nature (MedDRA PT), time to onset, duration, intensity, relationship to vaccination, and outcome of medically attended adverse events (MAAEs) that occur from vaccination 1 (Vac 1) until the end of the follow up period (12 months following the second vaccination visit).
- Occurrence, nature (MedDRA PT), time to onset, duration, intensity, relationship to vaccination, and outcome of AESIs that occur from Vac 1 until the end of the follow up period (12 months following the second vaccination visit).
- Occurrence, nature (MedDRA PT), time to onset, seriousness criteria, relationship to vaccination, and outcome of serious adverse events (SAEs) that occur from the Screening Visit (V0) until the end of the follow-up period (12 months following the second vaccination visit), and whether the SAE led to early termination from the trial
- Out-of-range biological test results at Days 8 and 30 after each vaccination and 15 days prior to the second vaccination in Part A and Days 8 and 30 after each vaccination in Part B, including occurrence, severity, timing, and relationship to vaccination

Efficacy

For participants in Part B (not conducted), to evaluate the efficacy of each of the investigational vaccine regimens with respect to:

- Relative change in HSV DNA detection frequency (shedding rate, as detected by polymerase chain reaction (PCR) conducted on self-collected swabs) between swabs collected before the first vaccination and those collected after the second vaccination visit
- Proportion of participants free of recurrence within the 6 months following the second vaccination visit.

Secondary Endpoints

Efficacy (For participants in Part B; not conducted due to study termination):

- The total number of days that the participants who receive investigational product or placebo report genital herpes lesions in the 6-month period following the date of the second vaccination visit
- The number of recurrences* within the 60-day swabbing period following the second vaccination visit (in participants who receive investigational product or placebo)
- Relative change in HSV DNA detection frequency (shedding rate, as detected by PCR conducted on self-collected swabs) between swabs collected before the first vaccination visit and those collected 60 days after the first vaccination visit plus after the second vaccination visit (in participants who receive investigational product or placebo)
- Relative change in HSV DNA detection frequency (shedding rate, as detected by PCR conducted on self-collected swabs) between swabs collected before the first vaccination visit and those collected 60 days after the first vaccination visit (in participants who receive investigational product or placebo)

*Recurrence is defined as the appearance of genital and perineal lesions (ie, blisters, ulcers) in a previously asymptomatic participant. Regarding 2 separate episodes of recurrences, recurrence is defined as the presentation of a new lesion (or lesions) after a 1-day-minimum (≥ 24 hours) lesion-free period.

Immunogenicity

- Change in serum HSV-2-antibody levels before and 30 days after the first and second vaccination visits and 6 months after the second vaccination visit
- Change in level of HSV-2-specific cellular immune responses before and 8 days after the first and second vaccination visits and 6 months after the second vaccination visit

Statistical methods:

Primary Safety

The number and percentage (with 2-sided 95% confidence intervals [CIs]) of participants in each group with each of the safety endpoints was to be computed. The exact binomial distribution (Clopper-Pearson method) for proportions was to be used in calculations of the 95% CIs.

Conduct of the study

eResearch Technology, Inc., commonly referred to as "ERT", was a contracted vendor for Sanofi during study HSV15. ERT provided Sanofi with medical devices and new online technologies such as smartphones, tablets, Web Apps and mobile Apps. These technologies permit Sanofi to collect clinical study data, such as pivotal endpoint data, patient reported outcomes (PROs), and Clinician Reported Outcomes.

On 20 September 2020, ERT encountered a cybersecurity attack. To avoid expansion of the attack, ERT proactively removed connectivity to and from the internet of all online systems while investigating the incident. This resulted in an outage period running from 20 September 2022 to 15 October 2022, without impact on safety or data integrity and no impact on study conduct.

Through the forensic analyses performed by ERT, there was no evidence to suggest that the malware attack impacted the core primary databases used to store clinical data that are collected for clinical trials. As a result, none of that data were impacted or exfiltrated. In addition, as the core clinical database systems were disconnected from the Internet, but never powered off during the incident, there was no risk of data loss associated with a system restart for these systems that host ERT's clinical databases.

With regards to the investigational plan, immediate consequences on study HSV15 were Enrollment interruption, Data transmission not received in the eCRF, Standard and Safety Notification offline (Medication entered alert, Severe Reaction alert and Other Reaction alert), ERT Clario portal not accessible.

The following measures were taken to mitigate impact on the study:

- Alterations in data collection and communications for participants enrolled prior to the outage:
- Alterations in enrollment procedures during the outage:
- Use of alternatives to ERT: Paper Diary Card distributed
- Quality control performed after system re-start to validate that data quality and integrity were maintained:

After event resolution and corrective measures implementation, the impact of this event on study HSV15 was evaluated as described below:

- Safety: no impact
- Data integrity: no impact
- Study conduct: no impact
- Conclusion on any adverse impact to the study: no impact

There were no major and critical protocol deviations directly linked to the ERT cybersecurity incident of 20 September 2022.

Summary Results:

Demographic and Other Baseline Characteristics:

Overall, equal proportion of male and female participants were enrolled in the study (50.0%). The mean age was 40.5 years (ranging from 27 to 55 years). It tended to be lower in Group 6 (33.5 years) compared with the other groups (ranging from 37.3 years in Group 3 to 45.0 years in Group 2). Twenty-one (75.0%) participants were White, and 7 (25.0%) participants were Black or African American. A total of 9 (32.1%) participants were Hispanic or Latino among all the included participants.

There were no meaningful differences between groups.

Exposure:

Of the 28 participants who were included, 4 were not randomized.

All randomized participants received Dose 1 in each group, and all received Dose 2, except 2 (50.0%) participants in Group 3 and 1 (25.0%) participant in Group 4. A total of 17 (60.7%) participants completed the visit at Day 240. The reasons for discontinuation were withdrawal by participant (8 [28.6%] participants) and loss of follow-up (3 [10.7%] participants). None of the participants completed the telephone call at Day 425.

Immunogenicity Results:

No immunogenicity data were obtained in this study.

Safety Results:

Immediate unsolicited AEs or adverse reactions (ARs)

Within 4 hours after any vaccination, none of the participants experienced any immediate unsolicited AE or AR.

Solicited reactions within 7 days after any vaccination

Solicited reactions were reported by 3 (75.0%) participants each in Groups 1 and 4, 4 (100.0%) participants each in Groups 2, 3, and 5, and by 2 (50.0%) participants in Group 6.

Solicited injection site reactions

Within 7 days after any vaccine injection, 3 (75.0%) participants in Groups 1, 3, and 4, and 4 (100.0%) participants in Groups 2 and 5 experienced solicited injection site reactions. There were no solicited injection site reactions reported in Group 6. After each vaccination, the occurrence rates of solicited injection site reactions remained comparable within each group.

The most frequently reported solicited injection site reaction after any vaccine injection was pain (75.0% to 100.0% across Groups 1, 2, 3, 4, and 5, and 0.0% in Group 6). Swelling was reported in 1 (25.0%) participant each in Groups 1, 2 and 3. Erythema was reported in 1 (25.0%) participant in Group 3. After each vaccination, pain remained the most common solicited injection site reaction.

In all groups (excluding Group 6 with no injection site reactions), most reactions were Grade 1 or 2, occurred within the first 3 days after vaccination, lasted 1-3 days and did not require any action to be taken. After each vaccination, most reactions remained of Grade 1 or 2. Only 1 (25.0%) participant in Group 2 experienced a Grade 3 reaction (swelling) after Vac 2 on Day 0. The reaction lasted 6 days and did not require any action to be taken.

Solicited systemic reactions

Within 7 days after any vaccine injection, 3 (75.0%) participants in Groups 1 and 4, 4 (100.0%) participants in Groups 2, 3, and 5, and 2 (50.0%) participants in Group 6 experienced solicited systemic reactions. The number of solicited systemic reactions tended to be higher after Vac 1 (50.0% to 100.0% across all the groups) compared with Vac 2 (33.3% to 75.0% across Groups 1, 2, 3, 4, and 5, and 0.0% in Group 6).

The most frequently reported solicited systemic reactions were myalgia (75.0% to 100.0% across Groups 1, 2, 3, 4, and 5, and 0% in Group 6), followed by malaise (25.0% to 75.0% across all the groups), headache (25.0% to 100.0% across Groups 1, 2, 3, 4, and 5, and 0.0% in Group 6), and arthralgia (25.0% to 75.0% across Groups 1, 2, 3, and 5, and 0.0% across Groups 4 and 6). After each vaccination, myalgia remained the most common solicited systemic reaction.

All solicited systemic reactions were Grade 1 or 2, and no Grade 3 reactions were reported. Overall, most reactions occurred within the first 3 days after vaccination, lasted 1-3 days and did not require any action to be taken. All episodes of fever required medication. After each vaccination, there were no differences between groups.

Unsolicited AEs and ARs within 30 days after any vaccination

Within 30 days after any vaccine injection, 1 (25.0%) participant in Groups 1 and 2, 2 (50.0%) participants in Groups 3 and 5, and 3 (75.0%) participants in Group 4 experienced unsolicited AEs. Unsolicited ARs were reported by 1 (25.0%) participant each in Group 1, 3, and 4, but none were reported in Groups 2 and 5. None of the participants in Group 6 reported any unsolicited AEs or ARs. After each vaccination, the number of unsolicited AEs remained comparable.

Most unsolicited AEs and ARs were Grade 1 or 2, occurred within the first 3 days after vaccination, and lasted 1-3 days or 4-7 days. After each vaccination, there were no differences between groups. One participant in Group 2 experienced a Grade 3 unsolicited AE of tibial fracture (also reported as an SAE, please see section "Other SAEs"). The most frequently reported unsolicited AEs were in the system organ class (SOC) "infections and infestations": both nasopharyngitis and oral herpes were reported by 1 (25.0%) participant in Group 3, and genital infection fungal by 1 (25.0%) participant in Group 4. In Group 5, 2 (25.0%) participants experienced genital herpes simplex, and one of them reported both furuncle and bacterial vaginosis.

There were only 3 ARs reported across all groups. Two ARs were in the SOC "general disorders and administration site conditions": 1 (25.0%) participant in Group 3 experienced injection site induration and 1 (25.0%) participant in Group 4 experienced injection site rash. One AR from the SOC "nervous system disorders" was reported by 1 (25.0%) participant in Group 1 (dizziness postural).

Deaths

There were no deaths reported during the study.

Other SAEs

During the study, 1 (25.0%) participant each in Groups 2 and 3 experienced an SAE (the SAE that occurred in the participant in Group 2 was reported within 30 days after vaccination). The SAEs were reported as follows:

- In Group 2, a participant reported tibial fracture due to road traffic accident 20 days after Vac 1. The event required hospitalization and was resolving at the date of last contact. It was considered as not related to the study vaccine.
- In Group 3, a participant experienced a pulmonary embolism 259 days after Vac 1. The event was life-threatening and required hospitalization. The event resolved 117 days after the onset. It was considered as not related to the study vaccine.

AEs leading to discontinuation

None of the participants experienced any AEs leading to study discontinuation during the study.

AESIs

None of the participants experienced any AESIs during the study.

MAAEs

During the study, MAAEs were reported in 2 (50.0%) participants in Group 1 and 1 (25.0%) participant each in Groups 2, 3 and 6 (the MAAE that occurred in a participant in Group 2 was reported within 30 days after vaccination). The MAAEs were reported as follows:

- In Group 1, a participant reported a Grade 2 COVID-19 on Day 80. The event lasted 15 days and required health care provider contact. It was considered as not related to the study vaccine.
- In Group 1, a participant reported a Grade 2 tooth infection on unspecified date. The event lasted 9 days and required both medication and health care provider contact. It was considered as not related to the study vaccine.
- In Group 2, 1 participant reported tibial fracture due to road traffic accident (see section “Other SAEs”).
- In Group 3, 1 participant experienced bacterial vaginosis of unknown intensity on Day 159. The event lasted 11 days and required both medication and health care provider contact. It was considered as not related to the study vaccine.
- In Group 6, 1 participant reported a Grade 2 hypoesthesia on Day 38, causing numbness of face, neck back and lower back. The event was still ongoing at the date of last contact and required both health care provider contact and medication. It was considered as not related to the study vaccine.

Laboratory parameters

Changes in laboratory parameters occurred in all groups during the study. Most biological measures were of Grade 1 or 2 maximum intensity, and Grade 3 biological measures were reported as follows:

- At V0, creatine kinase concentration was 845 IU/L for 1 (25.0%) participant in Group 5. The concentration decreased to 602 IU/L at an unscheduled visit before Vac 1 and returned to normal values (between 30-223 IU/L) before V02.
- At V03 (30 days after Vac 1), creatine kinase concentration increased to 983 IU/L for 1 (25.0%) participant in Group 5 and returned to normal values (between 38-234 IU/L) at V04 (15 days before Vac 2). The concentration increased again to 727 IU/L at V06 (8 days after Vac 2) and was normalized at V07 (30 days after Vac 2).
- At V03, creatine kinase concentration increased to 1146 IU/L for 1 (33.3%) participant in Group 4 and returned to normal values (between 30 223 IU/L) from V04 onwards.

These participants reported having physical activity prior to blood sampling, which likely contributed to increased creatine kinase concentrations.

Other results:

The COVID-19 pandemic had no impact on the integrity of the study. Adequate measurements were implemented by clinical sites in collaboration with the Sponsor to support participants during the study and to ensure the safe completion of visits and procedures.

Business Continuity Plans:

Business continuity plans (BCPs) were developed for the clinical study in order to define and monitor the measures to be implemented in response to the impact of the COVID-19 pandemic. A quality check was performed by the Clinical Quality Assessment team to validate that all key risks were considered and re-evaluated for impact in comparison to the original investigational plan, that there was a correlation between the identified study risks and the study specific BCPs, that contingency actions taken had proper documentation, and any expected reporting to Health Authorities / IRBs / ECs had occurred.

Changes in Planned Analyses Prior to Unblinding or Database Lock:

Due to early termination of the study, only main population and safety outputs have been produced.

Issue date: 15-Nov-2022