1. SYNOPSIS

Title of trial:

A multicentre, phase III, double-blind, randomised, parallel, placebo-controlled trial to assess efficacy and safety of early administration of Ivermectin during 3 consecutive days to prevent SARS CoV-2 (COVID-19) hospitalisation in adults older than 50 years of age

Trial number: IVER-303

EudraCT number: 2020-005015-40

Sponsor details: Chemo Research S.L., Manuel Pombo Angulo, 28, 28050 Madrid, Spain

Scientific and public contact points:

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Chief Scientific Officer

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Name of finished product: Ivermectin 9 and 18 mg, tablets

Name of active ingredient: Ivermectin

Investigators:

A total of 23 active centres in Spain (21 centres) and Slovakia (2 centres).

Coordinating Investigator:

José Muñoz Gutiérrez, MD, PhD, Hospital Clínic de Barcelona, C. de Villarroel 170, 08036 Barcelona, Spain

Publication (reference):

None.

Studied period (years):

date of first enrolment: 18-JAN-2021
date of last subject completed: 21-JUL-2021

No global interruptions and re-starts were reported.

Reporting period:

In Spain, this trial was prematurely stopped on 14-JUN-2021 due to a high vaccination rate in subjects older than 50 years. Globally, this trial was prematurely stopped on 21-JUN-2021 after performance of an interim analysis, dated 11-JUN-2021. Four last subjects were enrolled and randomised one day after (22-JUN-2021). All subjects who were enrolled in the trial could complete the trial. This report includes the data of the final analysis stage. For the reporting period, please refer to the dates of studied period.

Phase of development: Phase III

Background and rationale:

In late December 2019, an outbreak of the emerging coronavirus disease 2019 (COVID-19) began caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The epidemic was declared a pandemic by the World Health Organisation on 12-MAR-2020.

According to the World Health Organisation (WHO), as of 02-FEB-2022, 376 478 335 confirmed cases of COVID-19 were reported worldwide, with 5 666 064 confirmed deaths.

Even though some COVID-19 medicinal products (Kineret, Regkirona, RoActemra, Ronapreve, Veklury, Xevudy) or vaccines (Comirnaty, Nuvaxovid, Spikevax, Vaxzevria, COVID-19 Vaccine Janssen) are authorised by the EMA in the meantime, the timely evaluation of a safe and effective anti-viral agent that works by directly blocking the virus replication and is broadly efficacious against SARS-CoV-2 addresses a serious medical need. Ivermectin is an FDA-approved broad-spectrum antiparasitic agent that in recent years has shown antiviral activity against a broad range of ribonucleic acid (RNA) viruses *in vitro* in particular against SARS-CoV-2. The drug can be considered a host directed agent (HDA) which can reduce viral load by inhibiting a key cellular process that the virus hijacks to enhance infection by suppressing the host antiviral response. This change in the local environment causes less favourable conditions to the virus and, as a consequence, reducing viral load by even a modest amount by using a HDA at low dose early in infection can be key for enabling the body's immune system to begin to mount the full antiviral response before the infection takes the control. It is expected that high dose ivermectin should be sufficient to exert a significant antiviral activity on SARS-CoV-2. The proposed dose of 600 µg/kg/day for a longer period of treatment (5 consecutive days) in COVID-19 patients has shown an acceptable safety profile according to recent results from a proof-of-concept study performed in Argentina (Study IVM-AR-1 NCT04381884).

Objectives and Endpoints:

Primary objective: To assess the efficacy of early administration of ivermectin for three consecutive days to prevent SARS-CoV-2 hospitalisation in adults older than 50 years of age.

Endpoint: Percentage of subjects requiring SARS-CoV-2 hospitalisation during 28 days after first investigational product (IP) administration.

Secondary objective 1: To assess efficacy of an early administration of ivermectin for three consecutive days to prevent SARS-CoV-2 disease progression in adults older than 50 years of age.

Endpoint: Change in subjects' clinical status at Day 28.

Secondary objective 2: To evaluate the safety and tolerability of ivermectin in SARS-CoV-2 infected adults older than 50 years of age.

Endpoint: The occurrence of any adverse event (AE) related to ivermectin treatment.

Methods:

This was a multicentre, double-blind, randomised, prospective, placebo-controlled, parallel group clinical phase III trial in adult subjects older than 50 years of age, infected with SARS-CoV-2.

During screening/enrolment phase (Visit 1.1 to Visit 1.3) informed consent was obtained and the screening procedures were performed. A rapid antigen-based test was offered to all subjects who did not have a polymerase chain reaction (PCR) or a rapid antigen-based test result at screening (each of these tests could be considered a part of the standard procedure of the site). Eligible subjects were randomised 1:1 to receive ivermectin or placebo. The subjects received the IP, the dose was based on their body weight, and they took the first IP dose at site. The subjects received portable pulse oximeters for peripheral capillary oxygen saturation (SpO_2) monitoring at home. The treatment phase lasted 3 days and included an on-site Visit 1.3 and phone call Visits 2 and 3 which were performed on the following 2 days. PCR test or rapid antigen test results were communicated to subjects as soon as available. Subjects with a negative COVID-19 PCR test or rapid antigen test result were withdrawn from the trial unless they had a positive rapid antigen test or COVID-19 PCR test result a few days later. The subjects were followed up until Day 28.

During the follow-up, the subjects had phone call Visits 4 to 9 every other day, followed by Visit 10 after one week (Day 21). The subjects were asked to measure oxygen saturation as well as body temperature during all phone call visits and to report the respective results to the investigator. The on-site Visit 11 was the last visit (Day 28). The subjects were to return Ips (including empty and partially empty containers) and pulse oximeters.

In addition, the subjects were provided with a contact number available 24/7 to contact the investigator if their condition worsened. In case of health condition worsening (dyspnoea, fever [body temperature ≥ 37.8°C] lasting for more than 6 days, $SpO_2 \leq 95\%$ or any other worsening criteria based on the investigator's judgement) confirmed during the phone call visit, the subjects had an unscheduled visit at the site.

The subjects were to be hospitalised if they fulfil any of the following criteria: pneumonia confirmed by chest X-ray; $SpO_2 \leq 94\%$ or partial pressure of oxygen in blood (PO_2) < 80 mmHg in gasometry; respiratory frequency > 20 rpm; fever (body temperature ≥ 37.8°C) for more than 6 days plus one of the following analytic parameters: C-reactive protein (CRP) > 5 mg/dL, ferritin > 500 ng/mL or D dimer > 700 ng/mL. If there was any other condition that requires hospitalisation as per investigator judgement, the condition had to be documented in detail in the subject's file including a description whether the hospitalisation was performed due to SARS-CoV-2 infection.

Number of subjects (planned and analysed):

Planned: A sufficient number of subjects to have 832 randomised and 748 evaluable subjects

This trial was prematurely stopped.

Enrolled: 249	screened: 249	
screening failures: 4	randomised: 245	withdrawn: 17
completed: 228	analysed (safety): 244	analysed (efficacy): 244

Diagnosis and main criteria for inclusion and exclusion:

Male or female adult > 50 years of age with a SARS-CoV-2 infection diagnosed either through a rapid antigen-based test or an RNA based reverse-transcription polymerase chain reaction (RT-PCR) diagnostic test performed in nasopharyngeal sample were included in this trial. Initially, the onset of COVID-19 symptoms had to be less than 72 hours prior to screening.

Based on Protocol Final Version 3.0, 21-JAN-2021, the onset of COVID-19 symptoms was extended to be less than 120 hours (5 days).

Paediatric regulatory details:

Not applicable.

Measures of protection of subjects taken:

The subjects were closely monitored during the trial. Known life-threatening AEs caused by COVID-19 infection like venous thromboembolism and arterial thromboembolism were AEs of special interest and were considered important for the evaluation of the safety profile independent from the classification of seriousness, expectedness and intensity. The drug accountability was assessed regularly during the trial. Subjects who discontinued trial participation prematurely were asked to come to the site for an early discontinuation visit.

Test products, dose and mode of administration, batch number:

Ivermectin tablets (9 mg, 18 mg), oral administration.

Batch number: 20201101

Duration of treatment:

Three days.

Reference therapy, dose and mode of administration, batch number:

Placebo tablets (9 mg, 18 mg), oral administration.

Batch number: 20201101

The subjects received weight-based IP dose (test and reference) of 600 µg/kg every 24 hours.

The individual IP dose (test and reference) was as follows:

Body weight (kg) at screening	IP dose
50 to < 75	36 mg (= 2 x 18 mg) every 24 hours
75 to < 90	45 mg (= 2 x 18 mg + 1 x 9 mg) every 24 hours
90 to < 105	54 mg (= 3 x 18 mg) every 24 hours
105 to < 120	63 mg (= 3 x 18 mg + 1 x 9 mg) every 24 hours
120 to < 135	72 mg (= 4 x 18 mg) every 24 hours

Statistical methods:

The primary efficacy endpoint percentage of subjects requiring SARS-CoV-2 hospitalisation during 28 days after first IP administration was analysed using a two group χ^2 test.

The following statistical hypotheses were tested:

H_0: $p_I - p_P = 0$

H_1: $p_I - p_P < 0$

where pI represented the SARS-CoV-2 hospitalisation rate for ivermectin and pP the SARS CoV-2 hospitalisation rate for placebo.

The primary efficacy analysis was performed using the modified full analysis set (mFAS), this analysis was repeated with the full analysis set (FAS) and the per-protocol set (PPS).

All secondary efficacy endpoints were analysed with appropriate statistical methods using the FAS in an exploratory manner. Descriptive statistics was provided.

Treatment-emergent adverse events (TEAEs), clinical laboratory, vital signs, physical examination findings and other observations related to safety were analysed and reported in a descriptive way using the safety set (SAF).

The sample size was estimated assuming that an interim analysis with stopping criteria for early efficacy success was to be performed after 25% of subjects had completed the trial (or had clean primary endpoint data).

A total of 748 evaluable subjects (374 per group) was required to detect an odds ratio of 2.176 (for SARS-CoV-2 hospitalisation incidence of 7.5% in the ivermectin group and 15% in the placebo group) with 90.07% power and using a one-sided z-test with 2.5% significance level assuming variances were pooled and that continuity correction was not used. Assuming 10% drop out rate, 832 randomised subjects were required.

SUMMARY OF RESULTS

SUBJECT DISPOSITION:

A total of 249 subjects were enrolled at 23 trial centres in Spain and Slovakia. Of these, 244 subjects received at least one dose of IP including 125 (99.2%) IVER group subjects and 119 (100%) placebo group subjects (SAF/mFAS/FAS). The PPS comprised 98 (77.8%) IVER group subjects and 87 (73.1%) placebo group subjects.

A total of 59 (24.2%) subjects reported a major protocol deviation including 27 (21.6%) IVER group subjects and 32 (26.9%) placebo group subjects. Most frequently reported protocol deviation categories were additional study conduct deviations (47 [19.3%] subjects) and exclusion criteria deviations (13 [5.3%] subjects) with slightly lower percentages in the IVER group compared to the placebo group. From 12 (4.9%) subjects with treatment arm allocation deviations, 6 (4.8%) IVER group subjects and 6 (5.0%) placebo group subjects received a wrong IP kit number leading to 4 subjects receiving placebo instead of ivermectin and to 4 subjects receiving ivermectin instead of placebo.

A total of 228 (93.4%) subjects completed the trial (120 [96.0%] IVER group subjects and 108 [90.8%] placebo group subjects), and 16 (6.6%) subjects prematurely terminated the trial (5 [4.0%] IVER group subjects and 11 [9.2%] placebo group subjects). The most common primary reason for discontinuation were lost to follow-up including 3 (2.4%) subjects in the IVER group and 5 (4.2%) subjects in the placebo group.

The majority of SAF/mFAS subjects were of white race (240 subjects, 98.4%). The subjects' mean (SD) age was 59.2 (7.56) years and ranged from 50 to 84 years with similar age ranges and identical mean ages in both treatment groups.

The subjects' mean (SD) weight at screening was 78.88 (16.009) kg, mean (SD) height was 169.2 (9.38) cm and the mean (SD) body mass index (BMI) was 27.41 (4.713) kg/m^2 with similar data in both treatment groups.

The vast majority of trial subjects (72.5%) reported being non-smokers followed by ex-smokers (17.6%) and current smokers (9.4%) (SAF/mFAS/FAS). In the IVER group the percentage of smokers was slightly higher (11.2%) and the percentage of non-smoker slightly lower (70.4%) compared to the placebo group (7.6% and 74.8%, respectively).

In total, 69.7% of the subjects reported being alcohol abstainer (SAF/mFAS/FAS). The remaining subjects were moderate drinkers (28.7%) except for 1 subject (0.4%) who was an excessive drinker. In the IVER group, the percentage of abstainer was slightly lower (67.2%) and the percentage of moderate drinkers slightly higher (31.2%) compared to the placebo group (72.3% and 26.1%, respectively).

In total, all subjects had a positive SARS-CoV-2 infection diagnosis based on rapid antigen-based test or PCR test.

The most frequent ongoing medical history findings by preferred term were hypertension (27.0%), menopause (17.6%) and dyslipidaemia (16.0%). Frequency differences of more than 3.0% of subjects for a single preferred term between the treatment groups were observed for hypertension, hypercholesterolaemia, rhinitis and back pain with higher percentages in the IVER group compared to placebo and for asthma and chronic obstructive pulmonary disease with lower percentages in the IVER group compared to placebo.

The most commonly used concomitant medications in all subjects by substance name were paracetamol (82.4%), dexamethasone (24.2%) and omeprazole (22.1%). Frequency differences of more than 5.0% of subjects between the treatment groups with higher percentages in the IVER group were observed for omeprazole and acetylcysteine and with higher percentages in the placebo group for paracetamol.

The compliance to IP was high, 90.2% of subjects had a compliance between 80% and 120%. The mean (SD) compliance was 101.3 (11.92)%, the median compliance was 100%. The compliance ranged from 83% to 225%.

EFFICACY RESULTS:

The primary efficacy endpoint was the percentage of subjects requiring SARS-CoV-2 hospitalisation during 28 days after first IP administration. The primary efficacy analysis was performed using a two group χ^2 test in the mFAS, this analysis was also repeated with the FAS and the PPS. Hospitalisation rates of 34.4% (CI 26.1; 43.4) in the IVER group compared to 34.5% (CI 26.0; 43.7) in the placebo group led to a statistically non-significant treatment difference, an odds ratio (95% CI) of 1.002 (0.592; 1.699) (placebo vs. IVER) and a risk difference (95% CI) of -0.001 (-0.119; 0.117) (IVER vs. placebo). The same results were observed for the analysis on the FAS and similar (statistically non-significant) results for the PPS.

An additional analysis was performed for the mFAS, the FAS and the PPS using a logistic regression model with treatment group, gender and age group (50 to 59 and $\geq$ 60 years) as factors. A statistically significant age group effect was observed in the mFAS in favour of the younger subjects ($p = 0.0303$) leading to an odds ratio estimate (CI 95%) of 0.550 (0.320; 0.945) meaning that the probability of hospitalisation is lower in the younger age group. As expected, older populations were at higher risk of developing adverse complications as compared to their younger counterparts. [**Error! Bookmark not defined.**, **Error! Bookmark not defined.**] Also for the FAS but not for the PPS a statistically significant age group effect was observed.

The secondary efficacy endpoint was the change in subjects' clinical status at Day 28 determined according to the WHO clinical status assessment for COVID-19.

At baseline, all subjects were not hospitalised with the exception of 1 subject in each treatment group. Most subjects were not hospitalised, but able to resume normal activities (WHO scale 1) including 84.0% of subjects in the IVER group and 89.1% of subjects in the placebo group.

At endpoint the number and percentage of hospitalised subjects was 5 (4.0%) IVER group subjects and 4 (4.4%) placebo group subjects. More than 1 subject was only reported for WHO-8 scale 6 (hospitalisation, requiring intubation and mechanical ventilation) including 3 (2.4%) IVER group subjects and 2 (1.7%) placebo group subjects. A higher WHO-8 scale was only reported in the placebo group where 1 subject (0.9%) died (WHO-8 scale 8). For 2 other deaths including one per treatment group no WHO-8 questionnaire was completed. All other subjects

in both treatment groups were not hospitalised (95.9% in the IVER group vs. 95.8% in the placebo group). No relevant differences were observed between the mFAS and the FAS or the mFAS and the PPS.

Post-baseline, most subjects in the IVER group reported WHO-8 scale 1 and 2 (79.2%) as worst category. A total of 20.8% of subjects had a WHO-8 grade of 3 or higher corresponding to hospitalisation, most of them were categorised to WHO-8 scale 4 (8.8%), followed by WHO-8 scale 3 and 5 (4.0%, each) as worst category. Similar results were observed in the placebo group including 78.2% of subjects categorised to WHO-8 scale 1 and 2. A total of 20.1% of subjects had a WHO-8 grade of 3 or higher , most of them categorised to WHO-8 scale 4 (12.6%), followed by WHO-8 scale 3 (3.4%) and 6 (2.5%) as worst category. No relevant differences were observed between the mFAS and the FAS or the mFAS and the PPS.

An analysis of the number and percentage of subjects by worst post-baseline clinical status and age groups revealed a notably worse post-baseline status in the older age group compared to the younger age group. WHO-8 grades of 3 or higher corresponding to hospitalisation were reported for 13% younger IVER group subjects compared to 30.6% older IVER group subjects, most subjects were categorised in both age groups to WHO-8 scale 4 with 5.3% vs. 14.3%, respectively. In the placebo group, 17.3% younger placebo group subjects had WHO-8 grades of 3 or higher compared to 25.0% older placebo group subjects, most subjects were categorised in both age groups to WHO-8 scale 4 with 9.3% vs. 18.2%, respectively. No relevant differences were observed between the mFAS and the FAS or the mFAS and the PPS.

Only 4 (3.2) IVER group subjects and 4 (3.3%) subjects changed the WHO-8 scale category level by 3 levels or more.

SAFETY RESULTS:

The mean (SD) treatment duration was similar between treatment groups: 124 (99.2%) subjects had a treatment duration of 3 days in the IVER group compared to 116 (97.5%) subjects in the placebo group. The mean (SD) daily dose was also similar between treatment groups: 43.8 (8.82) mg in the IVER group vs. 45.6 (8.98) mg in the placebo group.

The percentage of subjects with **TEAEs** was slightly higher in the IVER group (108 [86.4%] subjects, 417 events) compared with the placebo group (101 [84.9%] subjects, 351 events). The most frequent individual TEAEs in total by preferred term were cough (70 subjects, 28.7%), pyrexia (56 subjects, 23.0%) and headache (51 subjects, 20.9%). Frequency differences of more than 3% of subjects for any individual MedDRA preferred term (PT) between the treatment groups with higher percentages in the IVER group compared to the placebo group were observed for cough, headache, diarrhoea, dizziness, vision blurred, dysgeusia and chest pain and with lower percentages in the IVER group for myalgia, abdominal pain and back pain.

The percentage of **TEAEs assessed as at least possibly related to trial treatment** was higher in the IVER group with 39 (31.2%) subjects compared to 29 (24.4%) subjects in the placebo group. The most related TEAEs in total by preferred term were reported for diarrhoea (15 subjects, 6.1%) and dizziness and headache (11 subjects, 4.5%, each). A frequency difference of more than 3% of subjects between the treatment groups with always higher percentages in the IVER group were observed for diarrhoea, dizziness and vision blurred.

The vast majority of TEAEs were classified as grade 1 (mild) or grade 2 (moderate) in intensity (77.9% and 29.1%, respectively), **TEAEs of grade ≥ 3 (severe or worse)** were reported for 18 (14.4%) subjects in the IVER group and for 15 (12.6%) subjects in the placebo group. The most common TEAEs by PT assessed as severe in the total population were pneumonia (21 subjects, 8.6%), COVID-19 pneumonia and respiratory failure (5 subjects, 2.0%, each). All

of these TEAEs are typical events for a COVID-19 infection. All other TEAEs with a grade ≥ 3 were reported in 1 to 2 subjects.

Three (1.2%) **deaths** were reported during the trial including 1 (0.8%) subject in the IVER group due to respiratory failure and 2 (1.7%) subjects in the placebo group due to COVID-19 pneumonia (1 subject) and pneumonia (1 subject).

The frequency of treatment-emergent serious adverse events (**TESAEs**) was low including 14 subjects (5.7%) who reported 16 TESAEs including 8 (6.4%) subjects in the IVER group and 6 (5.0%) in the placebo group. Individual TESAEs in total by preferred term reported in more than 2 subjects were pneumonia (2.5%) and respiratory failure (1.6%). Similar percentages were reported in both treatment groups for any individual TESAE. No TESAEs led to premature trial termination. One related serious TEAE (gastroenteritis) was reported in the IVER group.

No **TEAEs led to premature discontinuation** of the trial. No treatment-emergent adverse events of special interest (TEAESIs) of **venous thromboembolism (VTE) / arterial thromboembolism (ATE)** were reported.

For many **haematology and biochemistry laboratory parameters** and for all **disease biomarkers** abnormal results were reported at baseline and endpoint in above 10% of subjects in both treatment groups. Differences between the treatment groups of more than 5% of subjects with abnormal values at baseline or endpoint or differences within one treatment group of more than 5% of subjects with abnormal values at baseline and endpoint were only reported for a few parameters in both treatment groups.

The number of subjects with clinically significant abnormal haematology and biochemistry values (assessed by the investigator) was very low. In the IVER group, clinically significant abnormal values in no more than 2 subjects were reported at baseline for the haematology parameters white blood cell (WBC) count, absolute lymphocytes and platelet count and the biochemistry parameters triglycerides, alanine aminotransferase (ALAT) and lactate dehydrogenase (LDH) and at endpoint for the haematology parameter platelet count and the biochemistry parameters GGT and ALAT. In the placebo group clinically significant abnormal values in no more than 2 subjects were reported at baseline for the biochemistry parameters low-density lipoprotein (LDL) cholesterol and LDH and at endpoint for the biochemistry parameters ALAT and total protein.

Clinically significant abnormal parameters were only observed for disease biomarkers and not for haemostatic variables. In the IVER group, clinically significant abnormal values in no more than 3 subjects were reported at baseline for D-Dimer, ferritin and CRP, no clinically significant abnormal disease biomarkers were reported at endpoint. In the placebo group clinically significant abnormal values in no more than 2 subjects were reported at baseline for D-Dimer, ferritin and CRP and at endpoint for D-Dimer and CRP.

TEAEs based on individual laboratory abnormalities by preferred term which were reported in more than 1 subject were hyperglycaemia (2 subjects in both treatment groups) and hypokalaemia (3 IVER group subjects). One TEAE (chromaturia) in both treatment groups was judged to be related to the IP.

With regard to **vital signs**, almost all mean and median systolic blood pressure (SBP) values are above normal ranges at baseline and endpoint in both treatment groups. The mean and median values for all other vital sign parameters including diastolic blood pressure (DBP), pulse rate (PR), respiration rate, SpO_2 and body temperature are within normal ranges. No relevant mean or median changes in vital signs from baseline to endpoint were observed during the trial. The number of subjects with clinically significant abnormal vital sign results was very

low in both treatment groups. In the IVER group, no clinically significant abnormal values were reported at baseline and only for the parameters SpO_2 and temperature at endpoint (0.8% of subjects). In the placebo group a clinically significant SBP result (0.8% of subjects) was reported at baseline and for SBP and SpO_2 (0.9%, each) and respiration rate (1.0%) at endpoint. In summary, vital signs do not give any sign of safety concerns.

The number of subjects with clinically significant abnormal **physical examination** results was low in both treatment groups and do not give any sign of safety concerns.

In summary, ivermectin revealed no safety concerns as evaluated by laboratory parameters, vital signs and physical examination. With regard to TEAEs, comparable percentages were reported in both treatment groups with the exception of at least possibly related TEAEs with a higher incidence in the IVER group compared to placebo.

OTHER RESULTS:

Not applicable.

CONCLUSION:

The primary efficacy endpoint defined as percentage of subjects requiring SARS-CoV-2 hospitalisation during 28 days after first IP administration revealed no statistically significant treatment difference with hospitalisation rates of 34.4% in the IVER group compared to 34.5%in the placebo group. These results were confirmed by the FAS and PPS analyses.

An additional analysis based on a logistic regression model with treatment group, gender and age group (50 to 59 years and ≥60 years) as factors revealed a statistically significant age group effect in favour of the younger age group (mFAS and FAS). As expected, older populations were at higher risk of developing adverse complications as compared to their younger counterparts. [**Error! Bookmark not defined.**, **Error! Bookmark not defined.**] In the PPS no statistically significant age group effect was observed.

At baseline, nearly all subjects were not hospitalised (WHO-8 scale 1 and 2). At endpoint the number and percentage of subjects who had a WHO-8 grade of 3 or higher corresponding to hospitalisation was 4.0% in the IVER group and 4.4% in the placebo group. Post-baseline, most subjects reported WHO-8 scale 1 and 2 (not hospitalised) as worst category in both treatment groups with almost 80% (FAS). The percentage of subjects with worst WHO-8 scale of 3 to 8 was higher in the older age group. Only a few subjects in both treatment groups changed the category level by 3 levels or more.

In summary, ivermectin revealed no safety concerns as evaluated by laboratory parameters, vital signs and physical examination. An increased number of subjects with at least possibly related TEAEs with a higher incidence in the IVER group compared to placebo was observed and even the mainly mild intensity of these TEAEs which were reported in a relatively small number of subjects, makes it difficult to draw any robust conclusions.

Date of the report:

26-APR-2022