Declaration to the prematured end of the study EudraCT Nr. 2019-001151-40

Study title: Phase II pilot study: Determination of an effective and tolerable dose of Hylase® "Dessau" (bovine hyaluronidase) in the treatment of hyaluronic acid filler-induced overinjections by injection into defined hyaluronic acid filler-injected skin areas of healthy volunteers

Sponsor: RIEMSER Pharma GmbH Hohenzollerndamm 150-151, 14199 Berlin (Germany)

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Administrative information and trial identification:

Protocol No.: CTU148N

EudraCT Nr: 2019-001151-40

Study initiation date: 09/July/2019

Study completion date: 31/03/2020

Ethics committee(s): Lead EC: EC of Cottbus, Germany, EC of Hamburg, Germany

Name of test drug/product: Hylase® "Dessau" 150 I.U. (bovine hyaluronidase)

Trial design: The study was conducted as prospective, multicenter, randomized, single-blind, five-arm phase II pilot study.

Including criteria:

1. Male and female adults, age ≥ 18 - ≤65 years at the time of enrollment
2. Signed informed consent and ability to understand and follow the study instructions
3. Study participants were healthy and are in good physical condition
4. Heart frequency of > 50 - < 90 beats per minute and systolic blood pressure (BP) > 90 - < 140; diastolic BP > 50 - < 90 mmHg

Exclusion criteria: The exclusion criteria were defined according the current SmpC of Hylase Dessau (11/18)

Demographic information: 22 females and 6 males were included in the study. The mean age of the subjects of the ITT population was 49.5 years, range 21.0 – 65.0 years. The mean age of the subjects of the PP population was 50.0 years, range 20.0 – 65.0 years.

Objective(s) of the trial: The objective of the study was to determine a tolerable and effective dose of Hylase® "Dessau" (bovine hyaluronidase) as an antidote for the treatment of overcorrections by HA fillers based on the treatment of artificially induced overinjections on the back of the hands.

Outcome measures: Response to treatment was assessed by ultrasound and palpation.

Statistical methods: All data from the eCRF were included in the evaluation. The statistical evaluation of population related data was done descriptively. All efficacy analyses were performed for the ITT and PP set and separately for HA filler. The analytical methods are described in detail in a separate document (SAP - Statistical Analysis Plan) dated 07.05.2020. Statistical analyses were performed using SAS version 9.3 or higher (SAS Institute Inc., Cary, NC, USA).

Recruitment: Based on statistically calculations the study was originally planned with a number of 57 volunteers that have to be enrolled. Due to the premature end caused by the Corona pandemic only 28 volunteers could be included in the study.

Trial interruption: The trial was prematurely ended due to the pandemic situation in Germany caused by the Corona virus.

Adverse events: During this clinical study (from randomization to database closure) 27 AEs (17 ADRs after initial treatment, 2 ADRs after follow up injection, no SAE) were developed by 5 out of the 28 enrolled subjects. The ADRs were of mild intensity and only two ADRs were unexpected.

Conclusion: This study was performed to find an effective and safe dose of Hylase “Dessau” to treat overinjections caused by HA fillers. The study aim was not met due to the premature termination of recruitment. In summary, Hylase® “Dessau” was safe and well tolerated in the treatment of artificial HA filler overcorrection. Hylase® “Dessau” proved as a safe drug. Overall, no dose effect could be observed but all doses showed the desired effect achieving a volume reduction of at least 80.0% whereas after placebo injection a reduction of approximately 20.0% only was noted. It has to be taken into account that the low number of participants biased the results, so that further investigation including more subjects are warranted to establish statistical significance.