CLINICAL DATA

1. CLINICAL TRIAL KZHS2019

Name of the clinical test:	Use of HemaGel® SPRAY for the treatment of surface injuries of various aetiologies.
CT designation:	KZHS2019
CT sponsor:	VH Pharma a. s.
CT type:	Multicentric CT performed at three centres in the Czech Republic.
Objectives and justification of CT:	Verification of efficacy and safety of HemaGel® SPRAY in the treatment of superficial skin injuries in accordance with the intended use.
CT start date:	30 / 10 / 2019
CT end date:	28 / 2 / 2020
Number of enrolled subjects:	76
Number of adverse events:	0
Classification criteria:	Patients of the test centre with superficial injuries of the following types were enrolled as study subjects: - Cuts - Lacerations - Slashes - Abrasions - Torn skin, blisters - First and second degree burns - Dermatitis and sores caused by external causes - Maximum wound area up to 10 x10 cm - Age of patients over 18 years - Other wounds in subjects not meeting to the above criteria for wounds or patients with wounds reaching into the deeper layers of the skin, dermis, or wounds with a greater extent of damage than the stated maximum area, were not included into the clinical trial.
Exclusion criteria:	- if there was a significant worsening of the wound condition or pain parameter during the first week of treatment, or another worsening of the medical condition, e.g. in connection with hypersensitivity or a reaction to a component of the medical device previously not known - the beginning of a sentence or detention. - other necessary treatment that affected or biased the results of monitoring

Type of clinical test: multicentric, performed at 3 centres in the Czech Republic. Only the evaluated MD was used in this clinical trial for ethical reasons. **Common materials used by physicians in everyday practice and the common healing period of these injuries were used as comparators in the final evaluation.**

Evaluation and conclusions of KZHS2019:

Demography of subjects: groups of patients based on gender

Records of 76 subjects were statistically analysed, out of which 32 were male and 44 were female. The table below also lists patients based on indication/gender. The average age of patients was 47.6 years in males and 48.7 years in females.

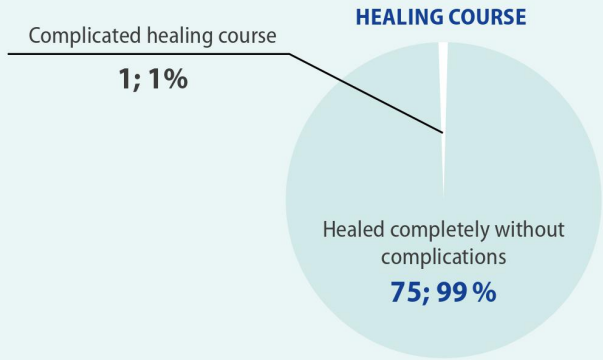
	CUTS, LASHES AND LACERATIONS	ABRASION, TORN SKIN, BLISTERS	FIRST AND SECOND DEGREE BURNS	SORES AND DERMATITIS	TOTAL NUMBER OF PATIENTS
Male	15	12	2	3	**32**
Female	11	12	17	4	**44**
Total	26	24	19	7	**76**

Assessment of the course of healing, incl. a graph and % values:

The case report form (CRF) allowed the physician to evaluate the course of healing process as follows.
- Healed completely without complications
- Complicated healing course

The course in 75 subjects was evaluated as "healed completely without complications" and one patient was evaluated as "complicated healing course".

The management in this patient followed the plan. But her general health, mental retardation and the location on the chin were associated with constant flow of saliva and self-harming. Therefore, the wound was fixed on day 8. At the final check-up, it was evaluated as almost healed with a certain prognosis of recovery.



	NUMBER OF PATIENTS	% EVALUATION
Healed completely without complications	75	98.68 %
Complicated healing course	1	1.32 %

A further distinction was made in patients with non-complicated healing course:

- Fully healed
- Almost healed with certain prognosis of full recovery

Out of 75 patients, 68 (90.66 %) patients were fully healed and 7 (9.33 %) patients were evaluated as certain prognosis of recovery.

Wound sizes in individual indications and evaluation of the healing course

In this clinical test, the wound size was already predefined in the inclusion criteria as a maximum of 100x100 mm. The size of the wound reached this maximum limit in almost all indications, with the exception of incisions, where the largest wound was 70 mm. Clinical practice also shows that the overall health of the patient, age and location of the injury were also important factors.

INDICATION(S)	SIZE OF THE WOUND IN mm	DETAILS ON THE COURSE OF HEALING
Cuts, lacerations and lashes	5 mm – 70 mm	These wounds are specific, mostly depending on the type of injury. Common knife cuts healed within a week, other lacerations-contusions required the application for two weeks, but the course was uncomplicated also here.
Abrasions, torn skin, blisters	5 mm - 100 mm	Completely without complications and fully healed. The fastest healing.
First and second degree burns	10 mm – 100 mm	Healing without complications. Minor injuries healed within a week, very nice effect in an oncology female patient after irradiation. Also in burns sustained during physiotherapy with hot paraffin and, last but not least, common scalds with tea, coffee or water.
Sores and dermatitis	20 mm – 100 mm	Extensive and neglected injuries. Despite this fact, almost all defects healed fully or to the stage with a certain prognosis of recovery.

Evaluation of the effect of evaluated MD on wound pain

Evaluation of pain was performed three times during the clinical testing, namely:

- Day one at the initial visit
- Day 5 – 7
- Day 14 at the final visit

At the initial visit, 55 subjects reported mild pain, 5 patients reported intermittent pain, and one patient experienced pain despite analgesics. A total of 80.3% of subjects reported pain.

However, during the first control assessment of pain between day 5 and day 7, 96% of subjects stated they were completely pain-free.

The above stated and also the verbal feedback of the investigators provided in the CRFs of individual subjects show that the evaluated MD reduces pain in the wound after the application within a few days of treatment start.

Evaluation of the effect based on the development of the wound environment

Although, the inclusion criteria allowed only superficial injuries – signs of redness around the wound at the initial visit were present in only 11 cases of the total 76. In two cases, this fact persisted until the final visit, but the physician evaluated these wounds as healed with certain prognosis of healing and without complications.

However, it is important to emphasise that the results of the clinical test confirmed that the application of the evaluated MD acts as a barrier against the entry of infection into the wound and thus the development of complications during the healing process or even the transition of the wound to chronicity. The most common cause of secondary healing is infection. There were no cases of wound condition worsening (reddening of the surroundings or other complications during healing) during the clinical testing.

Evaluation of the form of the product with respect to the application

As this new form of HemaGel® was developed not only to ensure safety and efficacy, but also to increase patient compliance mainly due to simplicity and convenience of application, CRF and the patient diary had a predefined application question as follows:

- Complicated (in what sense)
- Easy and comfortable

The application was easy and convenient in all 76 patients.

Evaluation of the product with respect to the frequency of application

The evaluated medical device was suggested for the application once every 24 hours, depending on the location or need. More frequent use is also possible. The frequency was verified as follows in the clinical practice:

	APPLICATION FREQUENCY 1x24 h	APPLICATION FREQUENCY 1x12 h
Cuts, lashes and lacerations	18	8
Abrasions, torn skin, blisters	21	3
First and second degree burns	13	6
Sores and dermatitis	7	
Total	59	17

The table shows that the proposed application once every 24 hours for the entire duration of the clinical trial was sufficient for 59 patients (77.6%). In 17 patients (22.4%), the application was reported twice in 24 hours, but a more detailed analysis of patient's diary showed that the application frequency returned to once every 24 hours in 5 patients of these 17 within 2–5 days. The remaining 12 patients of these 17 reported rather subjective sensations. E.g. left upper limb cutting injury – the female subject reported frequent hand washing and felt that the applied layer had to be washed away; another example was burns behind the ear and on the neck, rupture of a paraffin pad during physiotherapy session, the patient stated that the application was very pleasant, mildly cooling, so she wanted to experience that feeling more often.

Feelings immediately after application of the evaluated medical device

All 76 patients reported their immediate feelings after the application. 74 evaluated subjects stated no unpleasant sensations, sometimes positive perceptions, such as a pleasant feeling or mildly cooling sensation. Mild burning or itching was noted by two patients. This unpleasant feeling disappeared during the subsequent application in both cases.

As stated in the KZHS2019 plan, the study was performed only with the evaluated MD (i.e. without comparator) for ethical reasons and the investigators compared the efficacy and safety of the product with the existing recommended and available treatment on the Czech and European market. It is therefore important to put the above results in this context.

In general, the length of individual phases of acute wound healing is given as follows:

1. Exudative phase – 1 - 3 days.
2. Proliferation phase – 4 - 6 days.
3. Differentiation phase – from approx. day 7 – day 8, a few weeks.

These are the lengths of the process of the individual phases if there are no complications. In most cases, healing complications are caused by the entry of infection into the wound or by poor regenerative abilities of patient's tissue due to his/her poor health.

The average time to healing of all types of wounds in the clinical testing was 10.98 days during the use of the evaluated MD, despite the fact that 27% of subjects were over 55 years of age. Higher age is one of the key parameters influencing the quality of skin cover and the ability to heal. Based on the above, it can be confirmed that the evaluated product:

- Prevents infection entry into the wound
- Ensures a smooth healing process
- Accelerates healing of acute wounds
- It reduces the pain in the wound after the application
- The use of the evaluated MD is comfortable and increases the patient's compliance with the treatment

Final evaluation of KZHS2019 results

Based on the results and experience with the tested MD in the form of a spray at all three centres, the evaluated product seems beneficial for wound healing, especially for the management of superficial injuries of all types, including first and second degree burns and sores. The investigators provided only positive feedback of the evaluated MD in the comparison with the currently recommended and available treatment on the Czech and European market. The treatment went smoothly even in patients with a high-risk for complicated wound healing and no complications occurred at any stage of wound healing. The very suitable form of the MD supporting the patient's positive approach to the treatment is important as well.

CONCLUSION:

After the evaluation of all available data, including pre-clinical and clinical data from the three clinical test centres, HemaGel® SPRAY is safe and effective in clinical practice when used in accordance with the intended use and with the instructions for use.