Results Statement

Name of Sponsor/Company: Heidelberg University		**Sponsor-Code of Study:** MINDED	)
Name of IMP: Epiflex®, acelular human Dermis (ahD)		**Comparator:** VICRYL® (polyglactin 910) Netz (Standardtherapie)	
EudraCT-Nr.: 2015-001309-14			

Title of Study:

Comparison of the efficacy of using a human acellular dermis (Epiflex®) against the surgical standard procedure for closing an open abdomen with respect to avoiding ventral hernia.
A monocentric, controlled, prospective, partly-blind and randomized clinical phase III clinical trial

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1) Protocol versions during study period

Date of Version	Protocol Version	Changes
June 24th, 2016	Protocol V 3..0, Approval	Not applicable

2) Principal Investigator & Study Center

Prof. Dr. med. Peter Hohenberger
Universitätsmedizin Mannheim
Chirurgische Klinik, Sektion Spezielle Chirurgische Onkologie und Thoraxchirurgie
Theodor-Kutzer-Ufer 1-3
D-68167 Mannheim
Tel.: +49-621-383-2447
Fax: +49-621-383-1479

Study Center (monocentric study) & Ethic Committee:

Mannheim:
Prof. Dr. med. Peter Hohenberger
Chirurgische Klinik, Sektion Spezielle Chirurgische Onkologie und Thoraxchirurgie
Universitätsmedizin Mannheim
Theodor-Kutzer-Ufer 1-3
D-68167 Mannheim
Tel.: +49-621-383-2447
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3) Study period

First patient in: May, 9th 2017
Last patient in: March 6th, 2018
Registered End of Study: May 2nd, 2018

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4) Objectives & Endpoints

Primary hypothesis:
The efficacy defined by the avoidance of ventral hernia development when closing an open abdomen applying a human acellular dermis is higher than in case of applying an absorbable vicryl net.
Primary endpoint:
Primary endpoint is the evidence of ventral hernia 6 months after clinical trial surgical intervention by clinical examination, by abdominal sonification and by dynamic magnetic resonance tomography.

Secondary hypothesis:
The efficacy defined by the quality of life when closing an open abdomen applying a human acellular dermis is higher than in case of applying an absorbable vicryl net.
Secondary endpoints:
Secondary end point is the quality of life determined by EuraHS-QoL und SF-36 questionnaires and the evaluation of any implant complications (rupture, tears).

5) Study Design & Methodology

This study is a partly-blind, randomized, controlled, prospective and monocentric phase III study according to AMG. Patients were randomized to one of the two arms. IMP or Comparator was implanted (study intervention) followed by visits according to protocol.

6) Test product (IMP) definition, Reference therapy and mode of administrations

Treatment/study intervention consisted of the implantation of the IMP, the human acellular Dermis Epiflex®, manufacturer Deutsches Institut für Zell- und Gewebeersatz gGmbH (DIZG), 12555 Berlin, or, according to randomization's result, of the implantation of the Comparator, a VICRYL® (polyglactin 910) Netz, Manufacturer Ethicon Products, Johnson & Johnson MEDICAL GmbH, which was the standard procedure. For detailed information on the administration of p Epiflex® or VICRYL® (polyglactin 910) Netz please refer to the respective "Fachinformation".

Of the 4 patients enrolled until study termination, 1 of the patients was randomized to implantation of the IMP (Epiflex®), 3 of the patients to implantation of the Comparator (VICRYL® polyglactin 910 Netz).

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7) Number of patients (planned and analysed)

The planned number of patients to be enrolled in the trial was 50. Planned to be included into the study were patients within 'open abdomen' treatment in context with peritonitis with no possibilities to close the open abdomen by adaption of fasciae after finishing of Lavages.

Due to upcoming changes within the clinical treatment situation of ‚open abdomen' patients after study start (changing surgical concept), no additional patients could be enrolled into the study after patient No. 04 enrollment in March 2018. As changes in the enrollment situation towards a rising number of patients being eligible for inclusion were not expected and herewith planned subject number could not be expected to be achieved, the study was stopped on May 2nd, 2019, having enrolled 4 patients in total.

8) Results & Conclusion

Efficacy

Two of the enrolled four patients terminated study participation before Visit 4 (which is 6 months after trial surgical intervention for determination of **primary endpoint**)**,** so only two of the enrolled four patients can be evaluated according to the primary endpoint. Unblinding for information on the implanted product for evaluation purposes revealed both of the evaluable two patients having been implanted with the Comparator. One of them showed a clearly visible large hernia, the second patient showed no hernia in both sonography and MRT diagnostics.
As both of the evaluable patients with regard to the primary endpoint have received the Comparator and none of them the IMP, **the objective's first hypothesis cannot be evaluated.**

For efficacy in regard to the **secondary endpoint** concerning evaluation of any implant complications (rupture, tears) or Bulging 6 and 12 months after implantation of IMP/Comparator. Two of four enrolled patients attended Visit 4 and 5. Both of them having been implanted with the Comperator. None of the two patients eligible for evaluation of implant complications and Bulging showed any implant complications after 6 and 12 months. One of them showed Bulging grade 2 after 6 months, after 12 months MRT was not performed, so bulging was not determined. The other one showed Bulging grade 1 after 6 months no visible bulging after 12 months.

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The secondary end point further aimed to evaluate and compare quality of life with regard to the objective's second hypothesis. To aim for an evaluation of the above described a comparison between patients having been implanted with the IMP and patients implanted with the Comparator is mandatory. **As both of the evaluable patients have received the Comparator and none of them the IMP, the objective's second hypothesis cannot be evaluated.**

Safety

During study, 4 SUEs were reported, one for Patient ID 01, one for Patient ID 02, and two for Patient ID 03. None of the occurring SUEs were assessed to be related to the IMP or the Comparator implanted.

Conclusion

Due to only 2 evaluable patients and both of them having been Implanted with the Comparator as fixed by randomization's result, **an evaluation of both the primary and the secondary hypothesis is not feasible.**

Planned to be included into the study were patients within 'open abdomen' treatment in context with peritonitis with no possibilities to close the open abdomen by adaption of fasciae after finishing of Lavages. Due to upcoming changes within the clinical treatment situation of ‚open abdomen' patients after study start (changing surgical concept), no additional patients could be enrolled into the study more than 14 months after last patient's enrollment in March 2018. As changes in the enrollment situation towards a rising number of patients being eligible for inclusion were not expected, the study was stopped on May 2nd, 2019, having enrolled 4 patients in total.

The reasons for not having enrolled more patients into the study to end up in more evaluable patients and being able to compare patients with implanted IMP versus patients implanted with the Comparator came up after study initiation and could not be foreseen in study planning period and at study start. In a dynamic field of surgical methodology and treatment concepts with regard to as best defined interventions for patients changes of surgical concepts need to be considered and adapted to. As the changing surgical concept led to decreasing chances to find eligible patients for study inclusion, termination of the study was seen as a consequent and logical step to be taken.