CRANFLAP AAG-O-H-2043

CLINICAL INVESTIGATION REPORT
Study No: AAG-O-H-2043

Investigational Medical Device:	**CranioFix®2 system**
Device Class:	The instruments belong to the medical device class I, reusable surgical instruments for temporary application (FF103R, FF104R, FF105R) as well as non-invasive product (FF494R). The implants belong to the product group of neurosurgical cranial implants are classified in medical device class III as implantable device for long-term use in direct contact with the central nervous system.
Sponsor: **Name, Affiliation & Contact Details:**	Aesculap AG Am Aesculap-Platz 78532 Tuttlingen Germany Study Manager: Diana Kupferschmid Phone: +49 7461 95-31225 e-mail: Diana.Kupferschmid@aesculap.de
Coordinating Investigator: **Name & Affiliation:**	Not applicable
Principal Investigator: Name & Affiliation:	Minou Nadji-Ohl, Oberärztin Sektionsleitung Neuroonkologie und klinische Studien Neurochirurgie Katharinenhospital Klinikum der Landeshauptstadt Stuttgart gKAöR , Kriegsbergstrasse 60, 70174 Stuttgart, Germany Telephone: +49 711 278-01
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Indication Studied:	Fixation of craniotomized bone flaps and fractures to the neurocranium.
Study Design:	Prospective, single-arm, single center PMCF-study
Development Phase:	Post-Market. After CE-marking.
Study Initiation Date:	22.03.2022 (First Patient In, FPI)

Date of Early Study Termination:	Not applicable
Study Completion Date:	27.10.2023 (Last Patient Out, LPO)
Report Issue Date:	2024-09-24

Brief Synopsis

Title of Study:	Prospective, single center PMCF-study on the performance and safety of the CranioFix®2 system used for the fixation of craniotomized bone flaps and fractures to the neurocranium.
Investigators:	Minou Nadji-Ohl
Study Centre(s):	Klinikum Stuttgart – Katharinenhospital Neurochirurgische Klinik Kriegsbergstraße 60 70174 Stuttgart Germany
Publication (reference):	Not applicable
Studied period:	First patient in: 22.03.2022 Last patient out: 27.10.2023 Study period approximately 19 months.
Objectives:	To evaluate the performance of the CranioFix®2 system in daily clinical practice when used as intended, different safety and efficacy parameters were used. Primary endpoint was the postoperative stability of the bone flap after fixation.
Methods and study design:	Prospective, single-arm, single-center post-market clinical follow-up study under daily clinical routine.
Number of patients (planned and analysed):	Planned: 25 patients Recruited: 25 patients Analyzed: 25 patients
Diagnosis and main criteria for inclusion:	Inclusion criteria: Written informed consent Age ≥ 18 years Use of CranioFix®2 system according to IfU Planned postoperative MRI within clinical routine

	Exclusion criteria: Pregnancy Patients with hypersensitivity to metals or allergies to the implant materials Inflammations in the region of the implant site Bone conditions that rule out the application of CranioFix®2 titanium clamps Use with artificial cranial bone flaps Bone tumors in the area supporting the implant Degenerative bone diseases Missing dura mater Application in the facial skull (viscerocranium) and in the orbital or skull-base region Combination of implant components from different manufacturers, i.e. additional use of plates and screws on the same bone fragment
Test product	CranioFix®2 titanium clamp system consists of sterile CranioFix®2 titanium clamps for single use and reusable neurosurgical instruments for the application of titanium clamps. Implants: clamp Ø 11 mm (FF490T/FF490T-UNI) clamp Ø 16 mm (FF491T/FF491T-UNI) clamp Ø 20 mm (FF492T/FF492T-UNI) Instruments: CranioFix®2 cutting forceps / pin cutter (FF103R) CranioFix®2 removal forceps (FF104R) CranioFix®2 holding forceps (FF105R) CranioFix®2 applicator (FF494R)
Duration of treatment:	Study duration per patient about 3 months (±2 months)
Reference therapy:	Not applicable

Criteria for evaluation:

Clinical Performance / Efficacy:

Safety:

Primary endpoint: Stability of the bone flap after fixation, postoperative.

Primary variable: Planarity of the bone flap after implantation. Rate of the patients in which a dislocation of the bone flap occurs (defined as the height of tilting (depression / protrusion) greater than the bone width).

Secondary endpoints: Safety parameters:

Incidence of adverse events (intra- and postoperative, until follow-up) e.g. foreign body reactions, infections, injury to the dura, injury to the scalp, epiduralhaematoma, wound healing disorders. Special focus on (serious) adverse events with (possible) relation to the investigational product

Performance parameters:

Handling of CranioFix®2 system (intraoperative) on a Likert scale 1 to 5

Stability of the bone flap after fixation (intraoperative- and postoperative) on a Likert scale 1 to 5

Cosmetic outcome (intra- and postoperative) on a 3 point scale

Statistical Methods:

All data was analyzed descriptively by means of tables, figures, listings and statistical tests if appropriate. 95% confidence intervals were calculated for primary and secondary endpoint rates where appropriate.

SUMMARY - CONCLUSIONS

CLINICAL PERFORMANCE / EFFICACY RESULTS:

The aim of this observational study was to collect systematically and proactively data regarding the performance of the CranioFix®2 system, like adverse events (AEs), handling and cosmetic outcome, under daily clinical practice when used as intended by the manufacturer. The patients were followed up for 3±2 months.

The study included patients undergoing a surgery with fixation of craniotomized bone flaps and fractures to the neurocranium using the CranioFix®2 titanium clamp system.

In all 25 cases, the indication for the cranial repair was a tumor resection.

The procedures were performed by ten surgeons. The discharge and follow-up examinations were conducted by the previously defined investigative team.

The primary parameter was the postoperative stability of the bone flap after fixation. During all visits there were no negative evaluations given regarding the stability of the bone flap. The primary variable was the planarity of the bone flap after implantation, evaluated as the rate of the patients in which a dislocation of the bone flap occurred – defined as the height of the tilting (depression / protrusion) greater than the bone width. In 24 cases, the bone flap was assessed as "in level" either at the follow-up visit and/or at the discharge visit. The one patient for whom no assessment was given died after surgery before discharge.

The overall handling of the CranioFix®2 system was rated as "very good" (12 cases), "good" (12 cases) or "acceptable" (1 case) by the participating surgeons. In all cases there was no bad evaluation of the cosmetic outcome stated – neither by the surgeon nor by the patient.

SAFETY RESULTS:

Three AEs were reported, of which two were classified as serious adverse event (SAE).

In none of those cases a possible causal relationship to the CranioFix®2 system was determined.

In all three cases a probable causal relationship to the surgical procedure was determined.

CONCLUSION:

This study demonstrates that the CranioFix®2 system, used for the fixation of craniotomized bone flaps and fractures to the neurocranium, provides a safe handling and a firm and stable fixation of the bone flap with a good clinical and cosmetic outcome

Date of the report:

2024-09-24

Statistical analysis methods

All data was analyzed by means of tables, figures, listings and statistical tests if appropriate. The final programming was performed after closure of the database by use of the statistical software package SAS Viya software version V.04.00 (SAS Institute Inc., Cary, NC, USA).

All available data was analyzed.

For summarized results (e.g. mean, standard deviation), the number of used data is mentioned.

The patient data was identified by the patient ID assigned during data entry, which incorporates the study center ID.

The statistical analyses were performed according to following principles:

Variables with metric or ordinal scale were summarized with:

- Number of observations used (N)
- Minimum (Min)
- Maximum (Max)
- Median
- Mean
- Standard deviation (StD)
- (optional) 95% confidence interval of the median

Categorical variables were summarized with:

- Absolute frequency (n)
- Relative frequency (%)
- (optional) Nmiss
- (optional) 95% confidence interval of the relative frequency

A separate category "N/A" was used for missing values.

Missing data was analyzed as such and was not replaced by estimates.

Statistical figures and plots (e.g. box-plot, bar-chart) were presented where appropriate.

The statistical evaluation of the study data was carried out by the sponsor. A final biometrical report was set up.

The following tables inclusively descriptive statistics were planned,

- Demographic data
- Results
- AEs listing