Clinical evaluation of a new dual cure universal adhesive (Adhese Universal DC) in the indirect restorative therapy: A randomised, controlled clinical trial

Clinical Study Protocol

SHORT TITLE: Clinical evaluation of Adhese Universal DC in the indirect restorative therapy.

Study Type:	Randomised controlled clinical trial with Medical Device
Study Categorisation:	A
Study Registration:	Registry of the U.S. National Library of Medicine (http://www.clinicaltrials.gov): NCT04475679. Supplementary federal database (Portal for clinical trials in Switzerland - SNCTP, https://www.kofam.ch/en/snctp-portal/): SNCTP000004028. As soon as the new electronic system EUDAMED is operational, the clinical investigation will be retrospectively registered.
Study Identifier:	LL3615088 (CIP: LL3614643)
Sponsor, Sponsor-Investigator or Principal Investigator:	Ivoclar Vivadent AG Dr. med. dent. Carola Sonia Pentelescu Bendererstrasse 2 9494 Schaan Fürstentum Liechtenstein 
Investigational Product:	Adhese Universal DC
Protocol Version and Date:	Version 03 from 10.03.2021

Signature Page(s)

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The Sponsor-Representative and Principal-Investigator have approved the protocol version 02 (01.10.2020) and confirm hereby to conduct the study according to the protocol, current version of the World Medical Association Declaration of Helsinki, ICH-GCP guidelines or ISO 14155 norm if applicable and the local legally applicable requirements.

Sponsor-Representative:

Patrik Oehri

Place/Date Signature

Principal-Investigator:

Dr. med. dent. Carola Sonia Pentelescu

Place/Date Signature

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(ClinO, Appendix 3, 1.1, 2.1, 3.1, 4.1; Appendix 5, 2b)

Sponsor / Sponsor-Investigator	Ivoclar Vivadent AG
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Study category and Rationale	Category A According to Article 20 Categorisation of clinical trials of medical devices this clinical trial is a category A clinical trial since a medical device that has conformity marking will be used and the medical device will be used according to its instruction for use.
Clinical Phase:	n.a
Background and Rationale:	A post market clinical follow up study (PMCF) with Adhese Universal DC is planned to ensure the safety and efficacy of the product. It is a study with two arms. Inlays and onlays for molars and premolars will be luted with Adhese Universal DC or Adhese Universal.
Objective(s):	The null hypothesis is that there is a statistically significant difference between control and test group with respect to postoperative hypersensitivity. The secondary objective of this study is to assess the long-term clinical efficacy of the tested material when compared to the control in terms of marginal quality and retention/fracture rate of the restorations and vitality and fracture rate of treated teeth.
Outcome(s):	The primary endpoint of this RCT is the incidence rate of postoperative hypersensitivity. The secondary outcomes are the vitality and fracture rate of restored teeth and the retention/fracture rate of restorations.
Study design:	Randomised, control clinical trial – Equivalence study
Inclusion / Exclusion criteria:	The participants are aged between 18-65 years. The teeth included in the study show an indication for inlays/ onlays (defective restoration or decay), are vital, with healthy periodontium, and contact with at least one adjacent tooth and with an opposing tooth. Excluded from the study will be pregnant women, participants with known allergies to the used materials and/or local anaesthetics, participants with severe general diseases, participants with bad oral hygiene and high caries activity. Participants who suffer from symptoms of a SARS-CoV2 infection.
Measurements and procedures:	After information and written informed consent the participants will receive a dental treatment in relation to the restorative indication (caries, tooth/restoration fracture, insufficient restoration etc), which means that the inlay/ onlay cavity will be prepared and a digital impression with an intraoral scanner (Trios 3Shape) will be taken. Then, the cavities will be temporarily restored with provisional restorations. The scans and impressions will be sent to the lab where dental technicians will provide the final restorations made of lithium disilicate e.max CAD. In the following appointment the final restorations will be luted and final corrections as well as the finishing and polishing procedures will be done. The baseline recall will take place 7-10 days after the insertion of the restoration. At the baseline recall the study specific parameters will be evaluated according to the FDI Criteria ranging from 1 excellent to 5 clinically not acceptable. The recalls will be performed at 6, 12, 24, 36 and 60 months.

Study Product / Intervention:	Indirect restorations are bonded to the tooth surface by a dental adhesive. Dental adhesives can be light cured or dual cured. The latest generation of adhesives are universal adhesives. Additionally, a composite luting cement is used to fill the gap between tooth and restoration and to bond the restoration to the adhesive layer as well as the restoration. In the test group of the RCT Adhese Universal DC will be used in conjunction with the luting cement Variolink Esthetic. Adhese Universal DC is a new, universal, dual curing adhesive.
Control Intervention (if applicable):	In the control group Adhese Universal will be used in conjunction with the luting cement Variolink Esthetic. Adhese Universal is a universal, light curing adhesive which has been on the market for 6 years and has proven its clinical efficacy and safety.
Number of Participants with Rationale:	80 Teeth: 40 in the study group and 40 in the control group, at maximum two teeth per participant.
Study Duration:	6 years
Study Schedule:	September 2020 December 2026
Investigator(s):	Dr. Peschke Arnd, Benderer strasse 2, 9494 Schaan, Tel. [redacted] E-Mail: [redacted] Dr. Watzke Ronny, Benderer strasse 2, 9494 Schaan, Tel. [redacted] E-Mail: [redacted] Dr. Enggist Lukas, Benderer strasse 2, 9494 Schaan, Tel. [redacted] E-Mail: [redacted] Dr. Hu Ming, Benderer strasse 2, 9494 Schaan, Tel. [redacted] E-Mail: [redacted] Dr. Glebova Tatiana, Benderer strasse 2, 9494 Schaan, Tel. [redacted] E-Mail: [redacted]
Study Centre(s):	This RCT is a single centre study.
Statistical Considerations:	Non-parametric test (Mann-Whitney) between control and study group p=0.1 will be applied regarding the clinical parameters evaluated in this study. The sample was calculated using the G*power Software 3.1.9.7.
GCP Statement:	This study will be conducted in compliance with the protocol, the current version of the Declaration of Helsinki, the ICH-GCP or ISO EN 14155 as well as all national legal and regulatory requirements.

ABBREVIATIONS

Provide a list of abbreviations used on the protocol - to be completed

AE	Adverse Event
BASEC	Business Administration System for Ethical Committees, (https://submissions.swissethics.ch/en/)
CA	Competent Authority (e.g. Swissmedic)
CEC	Competent Ethics Committee
ClinO	Ordinance on Clinical Trials in Human Research *(in German: KlinV, in French: OClin, in Italian: OSRUm)*
eCRF	Electronic Case Report Form
CTCAE	Common terminology criteria for adverse events
DSUR	Development safety update report
GCP	Good Clinical Practice
IB	Investigator's Brochure
Ho	Null hypothesis
H1	Alternative hypothesis
HRA	Federal Act on Research involving Human Beings *(in German: HFG, in French: LRH, in Italian: LRUm)*
IMP	Investigational Medicinal Product
IIT	Investigator-initiated Trial
ISO	International Organisation for Standardisation
ITT	Intention to treat
MD	Medical Device
MedDO	Medical Device Ordinance *(in German: MepV, in French: ODim)*
PI	Principal Investigator
SDV	Source Data Verification
SOP	Standard Operating Procedure
SPC	Summary of product characteristics
SUSAR	Suspected Unexpected Serious Adverse Reaction
TMF	Trial Master File

STUDY SCHEDULE

(SPIRIT #13; ICH E6 6.4.2)

Study Periods	Screening	Treatment, Intervention Period		Follow-up					
Visit	1	2	3	4	5	6	7	8	9
Time (hour, day, week)	-60 days	2 hours	2 hours	7-10d	6 mon	12 mon	24 mon	36 mon	60 mon
Patient Information and Informed Consent	x								
Medical History	x								
In- /Exclusion Criteria	x								
Tooth Examination	x								
Pregnancy Test (only in case of uncertainty)	x								
Randomisation			x						
Vitality test	x	x		x	x	x	x	x	x
VAS for tooth sensitivity		x		x	x	x*	x*	x*	x*
Preparation of tooth, impression and cementation of provisional restoration		x							
Try-in and cementation of final restoration			x						
Use of Adhese Universal DC or Adhese Universal			x						
Primary Variables				x	x	x	x	x	x
Secondary Variables				x	x	x	x	x	x
Adverse events			x	x	x	x	x	x	x

x*: only for participants who suffer from any kind of postoperative hypersensitivity