Clinical Investigation Plan (CIP)

Clinical evaluation of a new dental glass ceramic in the indirect restorative therapy (one arm study)

Type of investigation:	clinical trial with Medical Device
Categorisation:	A1
Registration:	Registry of the U.S. National Library of Medicine (http://www.clinicaltrials.gov): NCT04933123. The trial additionally registers in the supplementary federal database (Portal for clinical trials in Switzerland - SNCTP, https://www.kofam.ch/en/snctp-portal/) with its submission on BASEC. Furthermore, as soon as the new electronic system EUDAMED is operational, the clinical investigation will be retrospectively registered, if required.
Identifier:	LL3945976 (CIP: LL3965040)
Principal Investigator and Sponsor, or Sponsor-Investigator:	Principal Investigator (PI): Dr. med. dent. Ming Hu Bendererstrasse 2 9494 Schaan Fürstentum Liechtenstein [redacted] Ivoclar Vivadent AG Bendererstrasse2 9494 Schaan Fürstentum Liechtenstein
Sponsor representative (if the Sponsor is not located in Switzerland)	Patrik Oehri, Senior Director Corporate Quality Management / PRRC [redacted]
Medical Device:	NEW DENTAL GLASS CERAMIC
CIP Version and Date:	Version 5.0 of 07.09.2021

Signature Page(s)

ID number of the investigation:	Study ID: LL3945976 Registries: Registry of the U.S. National Library of Medicine (http://www.clinicaltrials.gov): NCT04933123. The trial additionally registers in the supplementary federal database (Portal for clinical trials in Switzerland - SNCTP, https://www.kofam.ch/en/snctp-portal/) with its submission on BASEC. Furthermore, as soon as the new electronic system EUDAMED is operational, the clinical investigation will be retrospectively registered, if required.
Title:	Clinical evaluation of a new dental glass ceramic in the indirect restorative therapy (one arm study)

The Sponsor-Representative and the Principal Investigator have approved the CIP version [Version 5.0 07.09.2021], and confirm hereby to conduct the investigation according to the CIP, the current version of the World Medical Association Declaration of Helsinki, ISO14155 norm, ICH-GCP as far as applicable, and the local legally applicable requirements.

Sponsor-Representative:

Patrik Oehri

[redacted]

Place/Date Signature

Principal Investigator:

Dr. med. dent. Ming Hu

[redacted]

Place/Date Signature

This signature page is redundant as this is no multicentre clinical investigation.

Principal Investigator at the local investigational site*:

I have read and understood this CIP version [x (dated DD.MM.YYYY), make sure this corresponds to the CIP version and date in the footer], and agree to conduct the investigation according to the CIP, the current version of the World Medical Association Declaration of Helsinki, ISO14155 norm, ICH-GCP as far as applicable, and the local legally applicable requirements.

Site:	Name and address of site
Principal investigator at the local investigational site:	Printed name of Principal investigator

Place/Date	Signature

**Note: In multicentre investigations, this page must be individually signed by all participating Local Principal Investigators.*

<table>
<tr><td>Sponsor / Sponsor-Investigator</td><td>Ivoclar Vivadent AG</td></tr>
<tr><td>Title:</td><td>Clinical evaluation of a new dental glass ceramic in the indirect restorative therapy (one arm study)</td></tr>
<tr><td>Short title / Investigation ID:</td><td>Clinical evaluation of a new dental glass ceramic
Investigation ID: LL3945976</td></tr>
<tr><td>Clinical Investigation Plan, version and date:</td><td>Version 5.0 of 07.09.2021</td></tr>
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<tr><td>Category and its rationale:</td><td>Category A1
The medical device has conformity marking and will be used according to its instruction for use. The subjects are not subjected to any additional invasive or stressful procedures compared with those applied under normal conditions of use of the product.</td></tr>
<tr><td>Name of the MD, Unique Device Identification (UDI), name of the manufacturer</td><td>Name of the MD:
NEW DENTAL GLASS CERAMIC for CEREC/ inLab Neuer Glasskeramik-Block HT A3/ C14, HT A2/ C14, HT A1/ C14, Multi A1/ C14, Multi A2/ C14, Multi A3/ C14

Unique Device Identification (UDI):
<table>
<tr><th>Article</th><th>UDI</th></tr>
<tr><td>NEW DENTAL GLASS CERAMIC for CEREC/inLab HT A1 C14/5</td><td>DIVO7453711</td></tr>
<tr><td>NEW DENTAL GLASS CERAMIC for CEREC/inLab HT A2 C14/5</td><td>DIVO7453721</td></tr>
<tr><td>NEW DENTAL GLASS CERAMIC for CEREC/inLab HT A3 C14/5</td><td>DIVO7453731</td></tr>
<tr><td>NEW DENTAL GLASS CERAMIC for CEREC/inLab Multi A1 C14/5</td><td>DIVO7453681</td></tr>
<tr><td>NEW DENTAL GLASS CERAMIC for CEREC/inLab Multi A2 C14/5</td><td>DIVO7453691</td></tr>
<tr><td>NEW DENTAL GLASS CERAMIC for CEREC/inLab Multi A3 C14/5</td><td>DIVO7453701</td></tr>
</table>
Manufacturer: Ivoclar Vivadent AG
SRN number (Art. 31 MDR): LI-MF-000000522</td></tr>
<tr><td>Stage of development:</td><td>post-market stage with CE marking</td></tr>
</table>

Background and rationale:	A post market clinical follow up study (PMCF) with NEW DENTAL GLASS CERAMIC is planned to ensure the safety and efficacy of the product. It is a study with one arm. Inlays and onlays of NEW DENTAL GLASS CERAMIC for molars and premolars will be luted with Adhese Universal DC.
Objective(s):	The null hypothesis is that the survival rate of the inlays and onlays with NEW DENTAL GLASS CERAMIC is lower than 90% after 5 years. The secondary objective of this study is to assess the long-term clinical efficacy of the tested material in terms of aesthetic properties, functional properties and biological properties according to the FDI criteria.
Outcome(s):	The primary outcome of the study is the survival rate of this dental glass ceramic. The secondary outcomes are the surface lustre, surface and marginal staining, colour match and translucency, marginal adaptation, occlusal contour and wear, patient's view, postoperative (hyper-)sensitivity and tooth vitality, tooth integrity and adjacent mucosa.
Design:	Prospective one arm clinical trial
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), 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 (CEREC Primescan) will be taken. The dentists will design the restorations. The final design will be sent to a milling machine (CEREC Primemill) and milled. The polishing procedures will be done after milling. The final restorations will be luted adhesively. 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.
Intervention:	NEW DENTAL GLASS CERAMIC is a new kind of dental glass ceramic for indirect restorations. A crystallization process after milling is not necessary. It can be used for the fabrication of highly esthetic all-ceramic restorations using a CAD/CAM procedure.
Control intervention (if applicable):	n.a
Number of subjects with rationale:	44 teeth, at maximum two teeth per participant.
Duration of the investigation:	5 Years
Investigation schedule:	September 2021 January 2027

Investigator(s):	Dr. Peschke Arnd, Benderersstrasse 2, 9494 Schaan, [redacted] E-Mail: [redacted] Dr. Enggist Lukas, Benderersstrasse 2, 9494 Schaan, [redacted] E-Mail: [redacted] Dr. Pentelescu Carola-Sonia, Benderersstrasse 2, 949[redacted] E-Mail: [redacted] Dr. Hu Ming, Benderersstrasse 2, 9494 Schaar[redacted] E-Mail: [redacted] Dr. Glebova Tatiana, Benderersstrasse 2, 9494 Scha[redacted] E-Mail: [redacted]
Investigational Site(s):	This study is a single centre study: R&D Clinic Ivoclar Vivadent AG Benderersstrasse 2 9494 Schaan Liechtenstein
Statistical considerations:	Considering that the survival rate is studied, the sample size calculation is based on a binomial test since the survival rate is a dichotomous variable where the occurrences (survived, not survived) rather than the magnitude of an outcome are investigated. The calculation of the sample size is based on *Sample size calculations in clinical research* by Shein-Chung Chow[3] and yields a sample size of 44. A dropout rate of 10% is assumed. The expected survival rate is 90% or greater. Using this sample size, a power of 80% can be achieved at the 10% level of significance where the detection of an 8% difference is desired.
Compliance statement:	This investigation will be conducted in compliance with the CIP, the current version of the Declaration of Helsinki, ISO14155, ICH-GCP (as far as applicable) as well as all national legal and regulatory requirements.

ABBREVIATIONS

AE	Adverse Event
ADE	Adverse Device Effect
ASADE	Anticipated Serious Adverse Device Effect
ASR	Annual Safety Report
CA	Competent Authority (e.g. Swissmedic)
CEC	Competent Ethics Committee
CIP	Clinical investigation plan
ClinO	Ordinance on Clinical Trials in Human Research *(in German KlinV, in French Oclin, in Italian OSRUm)*
ClinO-MD	Ordinance on Clinical Trials with Medical Devices *(in German: KlinV-Mep, in French: Oclin-Dim, in Italian: OSRUm-Dmed)*
CRF	Case Report Form (pCRF paper CRF; eCRF electronic CRF)
DD	Device Deficiency
DMC / DSMC	Data Monitoring Committee, Data Safety Monitoring Committee

FDI	World Dental Federation (French: Fédération Dentaire Internationale)
Ho	Null hypothesis
H1	Alternative hypothesis
HRA	Federal Act on Research involving Human Beings *(in German: HFG, in French: LRH, in Italian: LRUm)*
IB	Investigator's Brochure
ICF	Informed Consent Form
ICH-GCP	International Council for Harmonisation – guidelines of Good Clinical Practice
IFU	Instruction For Use
ISF	Investigator Site File
ISO	International Organisation for Standardisation
ITT	Intention to treat
MedDO	Medical Devices Ordinance *(in German: MepV, in French: Odim, in Italian: Odmed)*
MD	Medical Device
MDR	Medical Device Regulation (EU) 2017/745 of 5 April 2017
PI	Principal Investigator
SADE	Serious Adverse Device Effect
SAE	Serious Adverse Event
SDV	Source Data Verification
SNCTP	Swiss National Clinical Trials Portal
SOP	Standard Operating Procedure
USADE	Unanticipated Serious Adverse Device Effect

SUMMARY OF THE REVISION HISTORY IN CASE OF AMENDMENTS

Version Nr, Version Date	Chapter	Description of change	Reason for the change
n.a.			

INVESTIGATION SCHEDULE

Study Periods	Screening	Treatment, Intervention Period		Follow-up					
Visit	1	2	3**	4	5	6	7	8	9
Time (hour, day, week)	-30 days	4 hours	1 hour	7-12d	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								
Vitality test	x	x		x	x	x	x	x	x
VAS for tooth sensitivity		x		x	x	x*	x*	x*	x*
Intraoral pictures		x		x	x	x	x	x	x
Preparation of tooth, intraoral scan, CAD/CAM procedures, try in of the restoration, adjustments and polishing, cementation of the restoration		x							
Post control, repolishing if necessary			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
Serious adverse events		x	x	x	x	x	x	x	x

Device deficiencies		x	x	x	x	x	x	x	x

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

x**: voluntary appointment