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Small-diameter titanium grade IV and titanium–zirconium implants in edentulous mandibles: Ten-year results from a double-blind, randomised controlled split-mouth core-trial

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Abstract

The goal of this extension study was to compare the 10-year outcome of 3.3 mm diameter titanium–zirconium (TiZr) or grade IV titanium (Ti) implants in mandibular implant-overdentures.

Materials and Methods: This study is the 10-year follow-up from a randomised, controlled, double-blind, split-mouth multicentre clinical trial. Patients with edentulous mandibles had received two implants in the interforaminal region (bone-level, diameter 3.3 mm, microrough surface), one of TiZr (test) and one of Ti (control). Implant survival and success, plaque and sulcus bleeding indices, probing pocket depth, gingival margin, clinical attachment level and radiographic crestal bone levels were evaluated.

Results: Fifty of 91 patients with implants were available for the 10-year examination and 36 patients were valid for the intent-to-treat (ITT) analysis. The implant success rate was calculated as 94.6% and 91.9% for the TiZr implants and the Ti implants respectively. Four implants were lost (TiZr = 1; Ti = 3) in the entire study period. Kaplan–Meier survival analyses estimated 10- year implant survival rate for TiZr to 98.9% and Ti 95.8%.The mean of total and functional crestal bone loss was 1.49 mm (±1.37 mm) and 0.82 mm (±1.09 mm) in the TiZr group and 1.56 mm (±1.34 mm) and 0.85 mm (±1.16 mm) in the Ti group.

Conclusions: This split-mouth design RCT on mandibular implant-overdentures evidenced, bearing in mind its follow-up time-related reduced cohort size, high 10-year implant success- and survival rates. These results confirm TiZr as well-suited implant material for realising small-diameter implants.

Registered on www.clinicaltrials.gov: NCT01878331.

KEYWORDS
overdentures, Roxolid, SLActive, split-mouth, Ti grade IV, TiZr

[†]See Appendix for the Roxolid Study Group.

1 | INTRODUCTION

Complete tooth loss continues to have a high prevalence in the older population, yet tends to develop at a later age (Hugoson et al., 2005; Norderyd et al., 2015). Complete edentulism in elderly patients is a challenge for the dental profession, as it requires a special age-adequate approach to treatment planning. Conventional dentures replace most of the lost structures, but cannot fully compensate functional impairment after tooth loss (Müller, 2014). Complete dentures treatment presents a number of disadvantages: hardships with stabilisation of the denture, especially in the mandible, incomplete recovery of chewing function with poor chewing efficiency and inability for patients to chew certain foods as well as speech difficulties. Patients often unconsciously adapt their food choice and limit their mandibular movements to the range which prevents denture displacement or pain. These shortcomings can affect the nutritional status and furthermore lead to avoidance of social contacts and a reduced quality of life (Müller, 2014). Over the time, as a denture is worn, physical retention decreases due to bone atrophy along with ageing and occlusal load bearing. As a rule, these problems are caused primarily by structural changes after atrophic changes in the alveolar bone and the inability to achieve sufficient stabilisation of classical complete dentures. Along with the increasing life expectancy, prospective planning is also required in view of a potential future functional decline which may render the patient dependent for the activities of daily living.

The implant mandibular overdenture with two interforaminal implants presents a multitude of functional and psycho-social improvements for the edentulous patient when compared to a conventional complete denture, which often falls short in fully restoring impaired oral function after tooth loss (Feine et al., 2002; Thomason et al., 2012). A number of scientific studies prove the positive impact on the level of patient satisfaction and quality of life of patients with implant-supported overdentures compared to conventional complete lower jaw dentures (Cardoso et al., 2016; Enkling et al., 2017; Kutkut et al., 2018; Yunus et al., 2016; Zhang et al., 2017).

However, achieving consent for implantation in elderly patients is often difficult, especially when there is a need for bone augmentation surgery to place implants of standard diameter. Therefore, special attention is focused on the possibility of treating edentulous patients with dentures supported by dental implants inserted without additional bone augmentation. Reducing the invasiveness of surgical interventions enhance achieving patient's consent for this type of treatment and lower the morbidity and cost of the treatment. One of the solutions is the placement of small diameter implants in edentulous areas of the jaw with insufficient bone volume of the alveolar ridge, in particular its width (Bielemann et al., 2019).

Encouraged by long-term success of implant-overdentures, the indications of endosseous implants are more and more extended to clinically challenging situations in terms of available bone volume for implant anchorage as well as compromised general health conditions (Engfors et al., 2004; Kowar et al., 2013). Progress in the implant surfaces has allowed for shorter healing times and improved osseointegration (Papaspyridakos et al., 2014; Schimmel et al., 2014). New TiZr alloys have been developed with improved mechanical properties which allow diameter-reduced implants being inserted even in clinically unfavourable anatomical conditions and thus further extend the indications for implant restorations (Marcello-Machado et al., 2018; Sohrabi et al., 2012).

The characteristics of the material and the implant surface are key factors for a successful outcome in modern implantology, because they not only influence the strength of the implant and its osseointegration but also a clinical performance and long-term clinical outcome (Fernandes et al., 2022; Ghazal et al., 2019; Hultin et al., 2020). TiZr alloy, which combines two materials with high biocompatibility, has already proven its best biomechanical force parameters. A chemically modified hydrophilic SLA surface can be created on TiZr implants, which promotes faster osseointegration compared to a normal SLA surface.

Titanium is considered the 'gold standard' for dental implants due to its corrosion resistance and biocompatibility, but titanium alloys containing zirconium show even better tensile and fatigue strength than pure titanium (Kobayashi et al., 1995). To increase the strength for small-diameter two-piece implants, TiZr alloy (Roxolid®; Institute Straumann AG, Basel, Switzerland) implants with the SLActive® surface have been introduced. 36-months' non-inferiority of Roxolid® implants was reported for mandibular overdentures in a multi-centre randomised controlled trial (Al-Nawas et al., 2012; Quirynen et al., 2015). Safety and long-term results after 60 months were already published (Müller et al., 2015). The present study aims to confirm the safety and long-term clinical performance in terms of implant survival and success, plaque and sulcus bleeding indices and radiographic crestal bone levels, Roxolid® implants after 10 years in the previously reported patient cohort provided with mandibular two-implant overdentures.

2 | MATERIALS AND METHODS

This study was designed as prospective 5- to 10-year follow-up of a randomised, controlled, double-blind, split-mouth, multi-centre clinical trial with a duration of 36 months in the core study. The materials and methods of the core study and the 5-year follow-up have been published previously (Al-Nawas et al., 2012; Müller et al., 2015; Quirynen et al., 2015). The 10-year follow-up study was conducted at six centres in four countries (Belgium, Germany, Italy and Switzerland). The study was performed in accordance with the Declaration of Helsinki and Good Clinical Practice (ISO 14155:2011) and approved by the Independent Ethics Committees of the coordinating investigator and all study centres. All participating patients gave their written informed consent. The study was registered at www.clinicaltrials.gov (NCT01878331).

2.1 | Patients and implants

Patients who had completed the core study were invited to participate in the follow-up study to collect long-term outcomes at 5 and 10 years after implant placement. The patients were selected according to predefined inclusion and exclusion criteria. The inclusion criteria were as follows:

- informed and written consent,
- treatment in the core study,
- completion of 36 month visit of the core study, and
- commitment to participate in the study until the 10-year follow-up examinations.

The exclusion criteria were as follows:

- physical handicaps interfering with the ability to perform adequate oral hygiene,
- conditions or circumstances, in the opinion of the investigator, which would prevent completion of study participation or interfere with analysis of study results, such as history of non-compliance or unreliability,
- use of any investigational drug or device during the study period.

All patients had presented with an edentulous mandible and had received two Straumann bone-level implants (Institut Straumann AG, Basel, Switzerland) in the interforaminal region, randomly allocated to one side in a double-blind, split-mouth design. The randomisation sequence had been computer-generated and the sequence been stored in sealed non-transparent consecutively numbered envelopes: They were only opened after the preparation of the osteotomy sites. Patients and examiners remained blinded to the allocation. Both implants had a diameter of 3.3 mm and a SLActive® surface. The test implant was fabricated from TiZr and the control implant from Ti, as defined in the core study (Al-Nawas et al., 2012).

2.2 | Surgical procedure

In the core study, surgery was performed under local anaesthesia following a standard surgical procedure. Implants of 8, 10, 12, and 14 mm length had been inserted and healing abutments had been installed to allow for trans-mucosal healing. Adequate bone height of at least 9 mm above vital structures in the intraforaminal region was required. The bone width allowed for the insertion of 3.3 mm implants without concurrent bone augmentation techniques. Sutures had been removed 1–2 weeks after surgery and the healing abutments had been replaced by Locator abutments (Zest Anchors LLC, Escondido, CA, USA) 6–8 weeks after implant placement. An implant-supported, removable overdenture had been placed within 2 weeks following abutment connection. The patients had attended follow-up visits at 6, 12, 24, 36, and 60 months. Patients from six centres who consented for the follow-up study were then recalled for the 10-year clinical visit.

2.3 | Implant survival and success

Implants still in place 10 years after surgery were counted as surviving implants. Adapted from the Buser criteria, implant success was defined as follows: The possibility for restoration, the absence of persistent patient complaints (pain, foreign body sensation and/or dysesthesia), the absence of recurrent peri-implant infection with suppuration, the absence of implant mobility and the absence of continuous radiolucency around the implant (Buser et al., 1990).

2.4 | Peri-implant bone level

Standardised panoramic radiographs were taken at baseline and 6, 12, 24, 36, 60, and 120 months after implant placement (Figure 1). Film-based images were digitised via video camera, light box and image analysis program (Brägger, 1998; Brägger et al., 2004) and digital images were analysed using ImageJ 1.33 open software (National Institutes of Health, Bethesda, MD, USA). The analysis of all images was performed by one independent expert (S.H.).

The known implant length was used as reference for the analysis. The reference line for the bone-level measurements was the implant chamfer 0.2 mm above the implant shoulder. The bone level was defined as the distance between the reference point and the first bone-to-implant contact (Figure 2). The mean value from mesial and distal measurements was used for analysis. The bone-level change was calculated as a function of the baseline level at implant placement. The peri-implant tissue was clinically judged with regard to its colour, consistency and surface morphology.

2.5 | Soft tissue assessment

Soft tissue assessment was performed at prosthesis placement and 6, 12, 24, 36, 60 and 120 months after implant placement by calibrated operators. Modified plaque index (mPI) and the modified

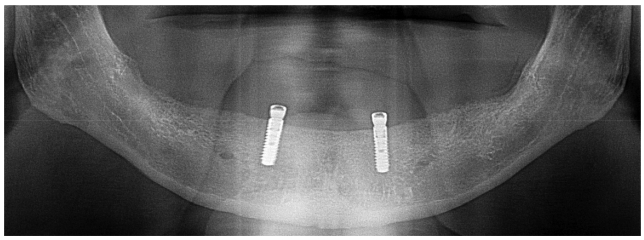

FIGURE 1 Radiograph showing test and control implant in the interforaminal region. The analysis was performed by an independent investigator using ImageJ software.

sulcus bleeding index (mSBI) according to Mombelli were recorded for the lingual, buccal, mesial and distal sites of the implant (Mombelli et al., 1987). In addition, probing pocket depths, gingival margins and clinical attachment levels were assessed.

2.6 | Oral health-related quality of life questionnaire

Oral health-related quality of life (OHRQoL) was measured per the Oral Health Impact Profile for Edentulous Patients (OHIP-Edent) (Allen & Locker, 2002). The questionnaire included 20 questions to be answered on a 6-point scale (worst score = 1, best score = 6).

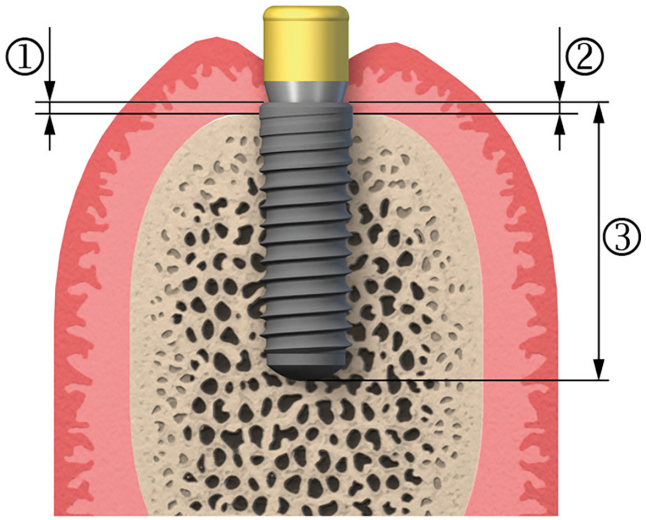

FIGURE 2 Illustration of the bone-level measurements. (1) Chamfer to first implant-to-bone contact, mesial (2) Chamfer to first implant-to-bone contact, distal (3) Length of implant. Müller et al. BMC Oral Health (2015) 15:123.

2.7 | Safety assessment

Patient safety evaluation included reporting of complications, adverse events (AEs), serious adverse events (SAEs) and device deficiencies. AEs and SAEs between 5- and 10-year follow-up were assessed for their relation to the study device and severity.

2.8 | Statistical analysis

Efficacy analysis was performed for implant survival and success, crestal bone-level change and soft tissue parameters up to 10 years after implant placement reported here based on the ITT data set. Comparisons between the test and the control groups were based on the corresponding 95% confidence intervals. Changes in crestal bone levels have been compared by *t*-tests between the treatment groups, and the *p*-values are of descriptive nature. Continuous data are presented as mean values (±standard deviation). For the analysis of crestal bone-level changes presented here, missing data were not imputed. Kaplan–Meier analysis was used to evaluate implant success and survival and the distributions were compared by log-rank tests. The 'safety data' enclose all enrolled patients, who received a study device during the core study and who entered the follow-up study.

3 | RESULTS

3.1 | Patients

Ninety-one patients were enrolled in the core study, of whom 75 patients completed the 36-month visit. When preparing the authorisation for the follow-up study, one centre had only one eligible participant, and it seemed unreasonable to obtain ethical approval for this single case. A further centre did not obtain ethical approval within the given time frame. Several patients could not be traced anymore, so that, finally 26 patients were not available. Finally, 49

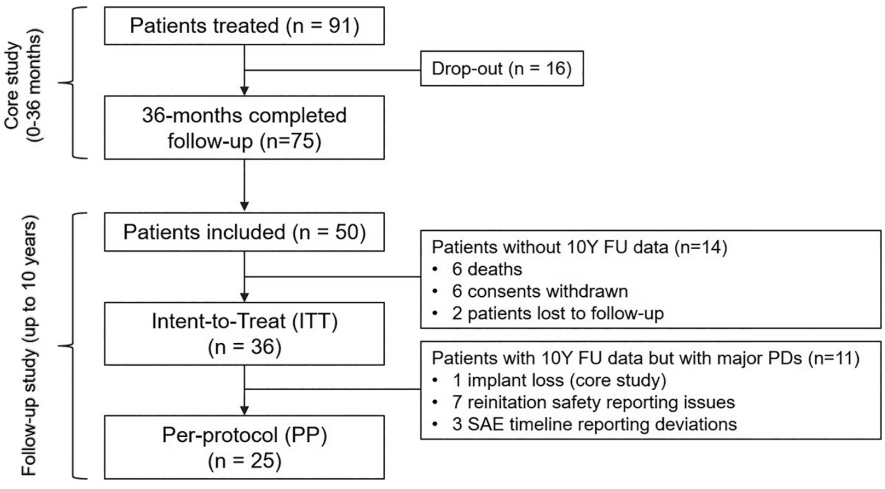

FIGURE 3 Patient flow diagram for the core (0–36 months) and the follow-up study (up to 60 months).

patients from the core study consented to participate for the 5 and 10 years of the follow-up study. One additional patient consented later to take part in the 10-year follow-up, therefore the total number of eligible patients amounted to 50. The recruitment for the follow-up period started in June 2013 and the last 10-year visit was performed in September 2018.

All 50 patients were eligible for participation, but 14 patients were excluded from the ITT analysis because of withdrawal of consent ($n=6$), death ($n=6$) and loss to follow-up ($n=2$), resulting in an ITT population of 36 participants. A further 11 patients were excluded from the PP analysis, because of safety reporting issues ($n=7$), SAE timeline reporting deviations ($n=3$) and replacement of a lost implant during the core study ($n=1$), providing a PP population of 25 participants (Figure 3).

The mean age of the ITT population at the 10-year follow-up visit was 76 ± 8 years (range 60–96 years). The patient demographic characteristics are presented in Table 1. The majority of patients (83.3%) suffered from clinically relevant diseases; among the most frequent ones were hypertension, surgeries for different reasons and hyperlipidaemia. Clinically relevant dental diseases were reported for 16.7% of the patients.

3.2 | Implant survival and success

3.2.1 | Primary analysis (implant survival)

The primary efficacy variable in this clinical study is implant survival assessed between baseline (surgery) and 10 years later. The ITT data set for the analysis of the 10-year follow-up data consists of 36 patients. However, for the evaluation of implant survival and success from one additional patient who consented later were considered. This patient lost his Ti implant in the 5- to 10-year follow-up period. Since no other data were available, this patient could not be considered for the regular ITT efficacy analysis, but for the evaluation of implant survival and success (extended ITT cohort, $n=37$).

Table 2 shows that in the extended ITT cohort of the 10-year follow-up analysis, two Ti implants were lost, leading to a survival rate of 94.6% (95% CI = 81.4% to 99.4%) in this group. The survival rate of TiZr implants was 100%.

TABLE 1 Demographic characteristics of the study population (ITT set).

	N	%
Gender		
Male	20	55.6
Female	16	44.4
Smoking status		
Non-smoker	23	63.9
Past-smoker[a]	13	36.1
Current clinically relevant disease		
Yes[b]	30	83.3
No	5	13.9

Note: Demographic patient data, 60 months after implant placement (ITT set, $n=36$).

[a]i.e. >10 cigarettes/day.

[b]Hypertension and hypercholesterolaemia.

3.2.2 | Implant success 10 years after surgery

Ten years after surgery, 94.6% of the TiZr implants and 91.9% of the Ti implants in the ITT analysis set were considered 'successful'. The 95% confidence intervals are widely overlapping, indicating no statistically significant difference between both treatments.

Reasons for non-successful implants during the 10-year follow-up visit were implant loss ($n=2$ in the Ti group), peri-implant infection with suppuration ($n=1$ in the TiZr group and $n=1$ in the Ti group) and pain, foreign body sensation, dysesthesia ($n=1$ in the TiZr group).

3.2.3 | Kaplan–Meier survival analysis for the entire study

Implant survival and success were additionally analysed from implant loading until the 10-year follow-up visit. A total of four implants were lost: 3 Ti and 1 TiZr implants (Figure 4).

Due to three implant losses during the first 3 months after implant loading, the overall probability for implant survival declined to 96.7% until that point in time and remained at this level until the end of the 10-year observation period. The overall probability for implant survival was dropped to 94.7% after 120 months because one patient lost his implant between 60 and 120 months. The mean overall survival time amounted to 116 months (95% confidence interval: 111–120 months).

The separate survival analyses for the two implant types showed the following: The cumulated probability for the survival of Ti and TiZr implants accumulated to 95.8% and 98.9% respectively. A log rank test, comparing these two probabilities showed no significant difference ($p=.31$). The mean overall survival times accumulated to 117 months (95% confidence interval: 113 to 122 months) for the Ti group and to 119 months (95% confidence interval 116–121 months) for the TiZr group, respectively. Kaplan–Meier curves for implant survival of the two different implant types over the entire 10-year observation period are shown in Figure 4.

In accordance with the survival analysis over the entire observation period, implant success was also evaluated from implant loading until the 10-year follow-up visit. Ten implants in nine patients were considered as 'non-successful': four TiZr implants and six Ti implants. A Kaplan–Meier analysis covering all treated patients over 10 years showed a probability for implant success of 85.4% over both treatment groups (93.8% for TiZr implants and 90.7% for Ti implants).

TABLE 2 Implant survival and success at 10-year follow-up visit (extended ITT set).

	TiZr (*N* = 37)		Ti grade IV (*N* = 37)	
Implant survival	***N***	**%**	***n***	**%**
Yes	37	100.0	35	94.6
No	0	0	2	5.4
95% confidence interval	n.a.		81.4–99.4	
Implant success	***N***	**%**	***n***	**%**
Successful	35	94.6	34	91.9
Not successful	2	5.4	3	8.1
95% confidence interval	81.4–99.4		78.0–97.9	

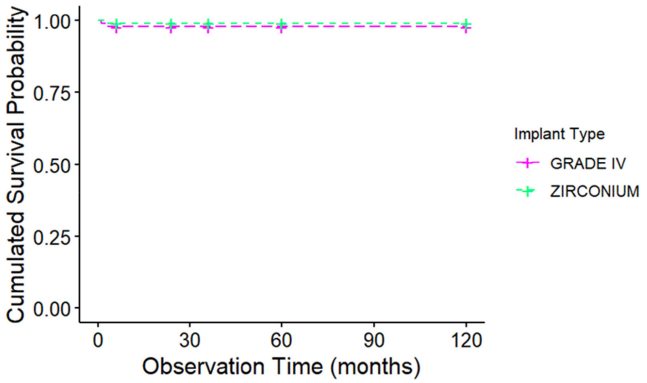

FIGURE 4 Kaplan–Meier Curve for implant survival over 10 years for the two implant types.

3.3 | Bone-level change

There were no notable differences in total crestal bone-level changes between the TiZr and the Ti groups, assessed 10 years after implant placement ($p = 0.837$). The mean change in the TiZr and Ti group was 1.49 mm (±1.37 mm) and 1.56 (±1.34 mm), respectively, ranging from −0.5 to 6.34 mm and from −0.31 to 5.51 mm, respectively, indicating a similar bone loss in both treatment groups.

Bone loss was observed in both treatment groups also with regard to the functional crestal bone levels with a mean change of 0.82 mm (±1.09 mm) in the TiZr group and of 0.85 mm (±1.16 mm) in the Ti group, ranging from −0.50 to 5.05 mm and −0.20 to 4.75 mm respectively. The changes are not significantly different between the treatments ($p = 0.910$).

Figure 5 shows the course of total and functional crestal bone levels over the entire observation period of the core and follow-up studies. The major part of bone loss occurred early after implant loading while the bone level remained almost unchanged between 3 and 5 years after surgery. Thereafter, it accelerated slightly between 5 and 10 year after surgery (Figure 5).

3.4 | Soft tissue assessments

The appearance of the soft tissue at the 10-year follow-up was 'physiological' in 83.3% of the TiZr sites and 82.9% of the Ti sites. The colour of the soft tissue was 'pink' in 86.1% of TiZr sites and 88.6% of the Ti sites. The tissue consistency was predominantly described as 'firm' for 66.7% of the TiZr sites and 68.6% of the Ti sites. The surface morphology of the soft tissue was 'smooth' in 63.9% of the TiZr sites and 62.9% of the Ti sites. The remainder was rated 'stippled' in both groups. Oral hygiene was rated 'excellent' or 'good' for 58.4% of the TiZr sites and 62.9% of the Ti sites.

3.5 | Other clinical measurements

Ten years after surgery, assessments resulted in the following:

The incidence of plaque (i.e. plaque index) at the different sites ranged from 30.6% to 44.4% for TiZr implants and from 28.6% to 45.7% for Ti implants.

The incidence of bleeding (i.e. sulcus bleeding index) at the different sites ranged from 16.7% to 30.6% for TiZr implants and from 20.0% to 28.6% for Ti implants.

The mean probing pocket depth ranged from 3.8 to 4.2 mm for TiZr implants and from 3.9 to 4.0 mm for Ti implants at the different sites around the implant.

The mean gingival margin ranged from 1.9 to 2.4 mm for TiZr implants and from 1.8 to 2.3 mm for Ti implants at the different sites around the implant.

The mean clinical attachment level ranged from 1.5 to 2.2 mm for TiZr implants and from 1.7 to 2.0 mm for Ti implants at the different sites around the implant.

The 95% confidence intervals for all clinical measurements were widely overlapping between the two groups indicating the absence of statistically significant differences.

3.6 | Patient-reported outcomes

The mean score of the OHRQoL questionnaire (OHIP-EDENT) over all 20 questions amounted to 5.49. The 95% confidence interval ranged from 5.26 to 5.77, indicating a very high OHRQoL.

3.7 | Safety

During the last 5 years of follow-up, in total, 59 AEs occurred in 31 out of 50 patients. The majority of AEs were biological complications (35.6%) such as peri-implant infections, recession, bone loss or pressure ulcers and technical complications (32.2%) such as fractures and other complications with the prosthesis. Six patients died due to reasons unrelated to the study. Twelve AEs were considered as

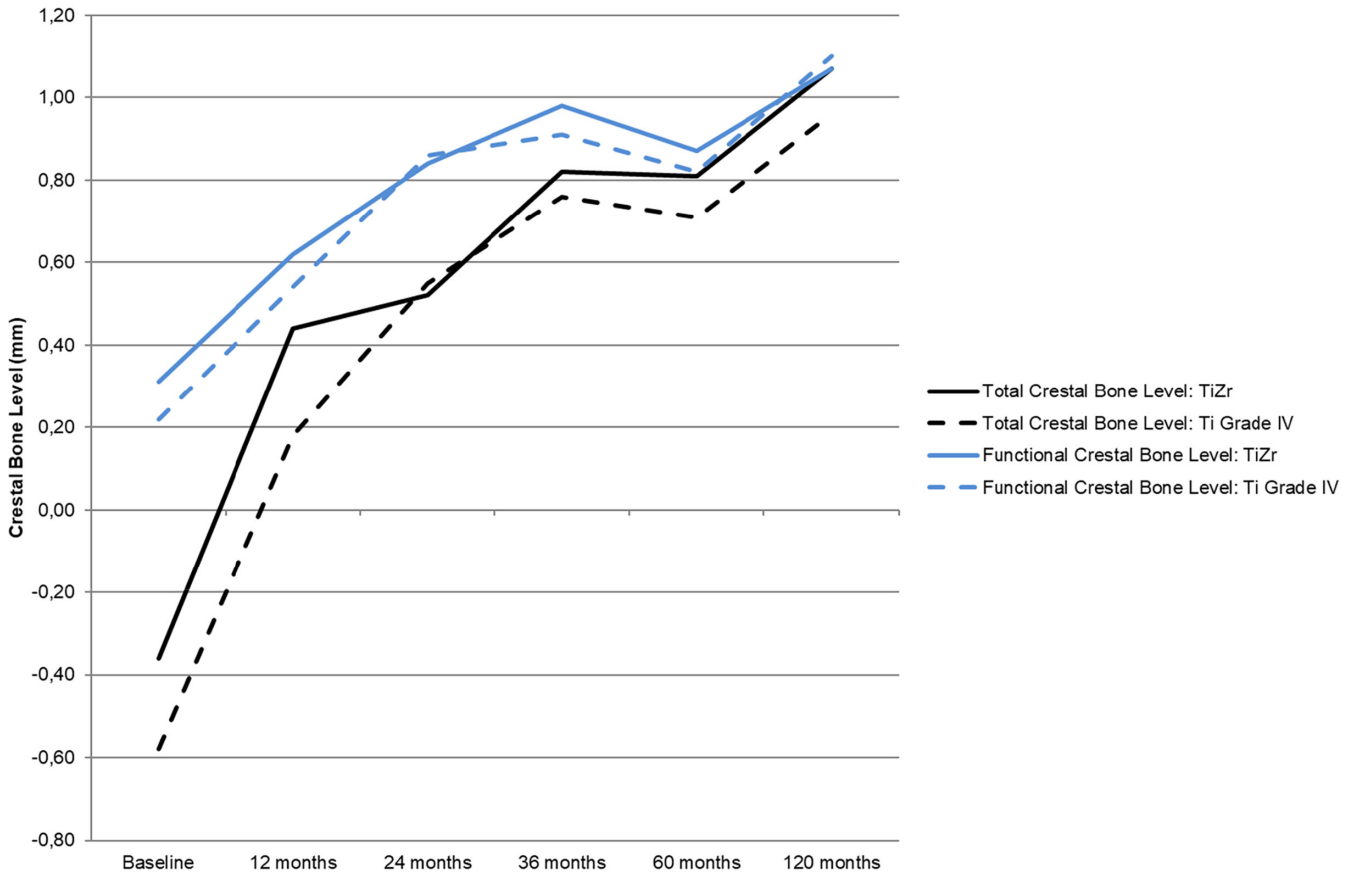

FIGURE 5 Total and functional crestal bone levels (mean) from baseline to the 10-year follow-up. Implants were categorised according to crestal bone-level change (ITT set).

serious, however, none of them was related neither to study device nor to study procedure. Neither additional complications nor device deficiencies have been observed.

4 | DISCUSSION

The use of osseointegrated implants to stabilise removable dentures on the lower jaw remains one of the great achievements of modern dentistry (Müller, 2014; Schimmel et al., 2017). The creation of a support from two dental implants for a removable denture on the lower jaw and its stabilisation reduces the extent of bone atrophy around the implants (Kremer et al., 2016), increases chewing efficiency (Enkling et al., 2017), reduces atrophy of the masseter muscles (Müller et al., 2012), and significantly improves the oral health-related quality of life (Müller et al., 2013). Today, the proposed standard of care for edentulous patients is an implant-supported overdenture anchored on two implants in the mandible to ensure patient satisfaction with the dental prosthesis over the long term (Müller, 2014).

The introduction of reduced-diameter implants expands the possibilities for implant placement in challenging clinical situations of severely atrophied edentulous lower jaw and narrow bone ridges when there is no sufficient bone resource for standard diameter implants placement and additional surgical intervention of bone augmentation is required. Small diameter implants (3.5 mm and less) have proven to be effective for overdentures in edentulous patients (LaBarre et al., 2008). In this case, two small diameter implants are sufficient support for the mandibular overdentures (El-Sheikh et al., 2012). The placement of small diameter implants without additional bone augmentation is an encouraging treatment option for patients avoiding additional surgical interventions and may contribute to their acceptance of treatment, reduce morbidity and lower the treatment cost (Hof et al., 2014; Pommer et al., 2014).

Although documented results of narrow implants for mandibular overdentures use are promising, studies evaluating long-term clinical results as well as oral health-related quality of life outcomes in patients receiving treatment with small-diameter implants are scarce.

The strength of this study is the follow-up period in an elderly population that extends to 120 months. Until to date, limited scientific evidence on the long-term survival of small-diameter implants in mandibular overdentures has been aggregated (Assaf et al., 2015; Marcello-Machado et al., 2018). In the present study, after 120 months' follow-up the cumulated probability for survival reached 95.8% and 98.9% for Ti and TiZr implants respectively. These survival rates are in line with earlier reported data. Assaf and co-workers summarised data from 17 studies on the outcomes of 1641 narrow diameter implants with an observation period of up

to 12 years and revealed the mean survival rate of 98.6% (Assaf et al., 2015). Marcello-Machado's meta-analysis based on collected data from 12 relevant studies on narrow diameter implants (790 implants in total) outcomes as mandibular overdentures retainers showed survival rate ranged from 80% to 100% (Marcello-Machado et al., 2018).

Long-term outcomes for small-diameter implants seem to be comparable or higher than the overall survival rate 92.5% and 85.9% reported for the standard diameter implants (Bakker et al., 2019) after 20 years follow-up and (Ueda et al., 2011) after 10–24 years, respectively. The average success rate was 96%, however, the reported long-term success rate was lower than short term (94% and 98% respectively). The long-term results might suggest that the longer the follow-up period the more implants are lost, but analysis of failures in the present study showed that they occurred mainly during the first year after placement. Specifically, a total of four implants were lost from implant loading time point until the 10-year follow-up visit. Three implant losses occurred during the first 3 month after implant loading resulting in the decline of overall probability for implant survival to 96.7%. One more implant failed in the period between 60 and 120 months and overall probability for implant survival was calculated as 94.7%. Early implant failures were also reported by other authors (Bakker et al., 2019; Patzelt et al., 2014; Riemann et al., 2019), suggesting a possible failure mode related to compromised osseointegration as opposed to other reasons associated with late failures, like, for example, occlusal overload or biological complications. Osteoimmunological in vitro studies analysing mesenchymal stem cell and macrophage behaviour have recently indicated that TiZr induced enhanced osteogenic and anti-inflammatory factor release by these cells when compared to Ti (Hotchkiss et al., 2017, 2019). Furthermore, these in vitro results corroborated with subtle differences in the in vivo healing kinetics leading to different qualities and potentially stronger bone around TiZr as compared to Ti implants (Galli et al., 2017; Jimbo et al., 2015; Kämmerer et al., 2014; Saulacic et al., 2012; Thoma et al., 2011; Wen et al., 2014). While these observations would explain lower early failure rates in TiZr implants, future in-depth studies will be required to substantiate a clear causal relationship between these different osteoimmunological properties of the investigated materials and implant survival (Albrektsson et al., 2019).

This study was planned and executed as a prospective, randomised, double-blind and split-mouth clinical trial comparing the clinical outcomes of using small diameter implants made of TiZr and implants made of Ti Grade IV as mandibular overdenture supports. One of the strengths of this study is the split-mouth design, which provides an identical biological environment to the test and control implant. Even the right- or left-handedness of a patient or the preferred chewing side is unlikely to have influenced the results, as the side-attribution of the test and control groups was randomised. Although the implants were made of different materials, their design, surface and diameter (3.3 mm) were common characteristics that made it impossible for the clinician to distinguish the implants visually. This unique opportunity formed the basis of the study design: two implants were placed in the mandible with random and double-blind allocation. According to the split-mouth design of this clinical research, the interforaminal space of the edentulous mandible of the study subject was divided into two experimental sites that were randomly assigned to the insertion of TiZr or Ti implants and each patient received implant treatment with both types of small diameter implants. This approach has a significant advantage due to the elimination of the influence of many inter-subject variabilities on the estimated treatment effect. Since the patient also serves as his/her own control, which generally increases statistical efficiency, fewer patients are needed for the study (Lesaffre et al., 2007).

After an observation period of 120 months, no significant differences in crestal bone-level change, clinical parameters, or survival and success rates were found between the groups. The outcomes seen at 12 as well as 36 months continued until 120 months, indicating that the outcomes of TiZr implants in this clinical setting were comparable to those in Ti implants.

Long-term observational studies are crucial when recommending a medical device for clinical use, even more so for elderly patients, where prosthodontic restorations should be designed for long-term survival, as renewal of prostheses and surgical interventions might become difficult with increasing frailty and multimorbidity. Adjustments which may become necessary to adapt the prosthodontic restoration to functional decline should rather be performed by a simple alteration of the denture to minimise the challenges to an elderly person's neuroplasticity and capacity of adaptation. Technical complications or failures in late life might be minimised when using only well documented and high-quality materials for dental restorations. Biological complications may still occur, as the overall risk of implant failure seems influenced by biological parameters like history of periodontal disease or residual periodontal pockets (Cho-Yan Lee et al., 2012; Zangrando et al., 2015) in addition to age-related changes, such as immunosenescence and a generally poorer level of oral hygiene. Patient behaviour such as smoking (Gruica et al., 2004) poor oral hygiene (Jepsen et al., 2015) or the absence of an adequate peri-implant width of keratinised and attached mucosa may also play a role. Technical aspects such as implant design and surface may also largely vary the clinical outcome, as was recently demonstrated in a large-scale industry-independent study on implant survival (Derks et al., 2015, 2016). In the latter study, the mentioned risk factors were confirmed, and in addition, implant length and implant brand were identified as relevant factors for long-term implant survival and success.

The present data confirm that Roxolid® implants were comparable to the traditional Grade IV titanium alloy in 3.3 mm diameter implants for an implant-supported mandibular overdenture over a 10-year period. This confirmation is of particular importance with regard to the above-mentioned concern about safety and quality of implant materials in pre-elderly and elderly patients. The peri-implant bone loss, modified Plaque Index, modified Sulcus Bleeding Index as well as implant success and survival are not statistically different between the two implant materials, confirming that the test group did not perform inferior to the control group. In this noninferiority study both ITT and per-protocol analyses of clinical outcomes

have been conducted. Applying of the intention-to-treat ITT principle is important for estimating the efficacy of treatment that is clinically relevant.

However, any clinical study has inherent inconsistencies, as one patient may vary from the other in a multitude of aspects, especially at an advanced age where the prevalence of chronic diseases increases. A further substantial shortcoming is that not all of the 91 patients who originally received implants were available for all follow-up visits. The core study was planned for 36 months, and ethical permission and insurance had expired after this follow-up period and renewal was necessary. One centre had only one participant recruited, and it seemed unreasonable to undergo the effort of study submission to the Ethics Committee for this single case. A further centre did not obtain ethical approval in time. Consequently, 26 patients were lost for recruitment for the present study. A worst-case implant survival rate was therefore calculated at 53.8%. However, knowing that 10 patients were not included for formal reasons, and considering that the included patients did not differ statistically from the not-included participants from the core study at baseline as well as at 12-month, 24-month and 36-month follow-up, it seems reasonable to assume that this worst-case scenario is unrealistic. The crestal bone-level changes reported in the present study are within the range reported in the literature for similar clinical indications. A recent meta-analysis on marginal bone-level changes at dental implants after an observation period of 60 months concludes that the annual bone level in the present study below or much below what hitherto has been reported (Laurell & Lundgren, 2011). The change in total crestal bone level noted in the present patient cohort after 10 years was 1.49 ± 1.37 mm for the TiZr group and 1.56 ± 1.34 mm in the Ti group respectively. The reported bone-level changes after 60 months are in between the one reported by Laurell end Lundgren for the Straumann Dental Implant System (0.48 mm (95% CI −0.598, −0.360) and the Brånemark System with 0.75 mm (95% CI −0.802, −0.693). When comparing these results with the ones from the meta-analysis, it has to be born in mind that both, elderly and edentulous patients are at particular risk for poor oral hygiene. Around one-third of this study's patient cohort did present with modified Plaque Index and modified Sulcus Bleeding Index scores above zero. However, little is known on the impact of biofilm on the peri-implant bone level (Salvi et al., 2017), especially for elderly patients with an aged immune system. The relation between peri-implantitis and oral hygiene will be of increasing importance for the dental profession, as a growing number of patients with implants will age, hence poor oral hygiene seems pre-programmed.

The benefits of implant overdentures for edentulous patients are well documented and the cost-effectiveness of this treatment protocol has been demonstrated (Feine et al., 2002; Thomason et al., 2012; Vogel et al., 2013). Compared to conventional dentures, the chewing efficiency may be significantly improved, given that new implant-supported removable overdentures are manufactured (Van Der Bilt et al., 2010). The chewing muscles seem more trained due to the improved chewing performance and after stabilising a lower denture by means of implants the muscle bulk can be re-gained, even in very old adults (Müller et al., 2012). The benefits of mandibular overdentures on oral function have recently been summarised in a systematic review (Srinivasan et al., 2023).

Further improvements of overdentures compared to conventional complete dentures comprise denture satisfaction and oral health-related quality of life (Awad et al., 2014; Rashid et al., 2011), although these outcome measures are complex and may vary between cultures and personalities (Awad et al., 2014). Elderly persons are in general less demanding concerning an improvement of their denture performance (Müller et al., 1994; Steele et al., 2004), yet do in general appreciate an improvement of their chewing performance (Øzhayat & Gotfredsen, 2019). Nevertheless, around one-third of edentulous patients reject implant insertion because they object the surgical intervention (Walton & MacEntee, 2005). Low-diameter implants may not only have a positive effect on the preservation of the residual alveolar ridge and therefore be biologically favourable in certain clinical situations. They may also avoid invasive bone augmentation procedures (Al-Nawas et al., 2015) whereby patient's morbidity as well as treatment costs and time can be reduced significantly (Sohrabi et al., 2012) and the smaller the intervention, the more likely is the acceptance in edentulous patients.

This split-mouth design RCT on mandibular implant-overdentures evidenced, bearing in mind its follow-up time related reduced cohort size, high 10-year implant success and survival rates. These results confirm TiZr (Roxolid) as a well-suited implant material for realising small-diameter implants.

AUTHOR CONTRIBUTIONS

FM and MS prepared the manuscript. All authors contributed to this clinical trial, that is, study design, study conduct, data collection and review of the manuscript. All authors approved the manuscript prior to submission.

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CONFLICT OF INTEREST STATEMENT

The authors have no conflicts of interest to declare. A moderate per capita remuneration was received by the institution per completed CRF.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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REFERENCES

Albrektsson, T., Becker, W., Coli, P., Jemt, T., Mölne, J., & Sennerby, L. (2019). Bone loss around oral and orthopedic implants: An

immunologically based condition. *Clinical Implant Dentistry and Related Research*, *21*, 786–795.

Allen, F., & Locker, D. (2002). A modified short version of the oral health impact profile for assessing health-related quality of life in edentulous adults. *The International Journal of Prosthodontics*, *15*, 446–450.

Al-Nawas, B., Brägger, U., Meijer, H. J. A., Naert, I., Persson, R., Perucchi, A., Quirynen, M., Raghoebar, G. M., Reichert, T. E., Romeo, E., Santing, H. J., Schimmel, M., Storelli, S., ten Bruggenkate, C., Vandekerckhove, B., Wagner, W., Wismeijer, D., & Müller, F. (2012). A double-blind randomized controlled trial (RCT) of titanium–13Zirconium versus titanium grade IV small-diameter bone level implants in edentulous mandibles–results from a 1-year observation period. *Clinical Implant Dentistry and Related Research*, *14*, 896–904.

Al-Nawas, B., Domagala, P., Fragola, G., Freiberger, P., Ortiz-Vigón, A., Rousseau, P., & Tondela, J. (2015). A prospective noninterventional study to evaluate survival and success of reduced diameter implants made from titanium–zirconium alloy. *The Journal of Oral Implantology*, *41*, e118–e125.

Assaf, A., Saad, M., Daas, M., Abdallah, J., & Abdallah, R. (2015). Use of narrow-diameter implants in the posterior jaw: A systematic review. *Implant Dentistry*, *24*, 294–306.

Awad, M. A., Rashid, F., Feine, J. S., & Overdenture Effectiveness Study Team Consortium. (2014). The effect of mandibular 2-implant overdentures on oral health-related quality of life: An international multicentre study. *Clinical Oral Implants Research*, *25*, 46–51.

Bakker, M. H., Vissink, A., Meijer, H. J. A., Raghoebar, G. M., & Visser, A. (2019). Mandibular implant-supported overdentures in (frail) elderly: A prospective study with 20-year follow-up. *Clinical Implant Dentistry and Related Research*, *21*, 586–592.

Bielemann, A. M., Marcello-Machado, R. M., Schuster, A. J., Chagas Júnior, O. L., Del Bel Cury, A. A., & Faot, F. (2019). Healing differences in narrow diameter implants submitted to immediate and conventional loading in mandibular overdentures: A randomized clinical trial. *Journal of Periodontal Research*, *54*, 241–250.

Brägger, U. (1998). Use of radiographs in evaluating success, stability and failure in implant dentistry. *Periodontology 2000*, *17*, 77–88.

Brägger, U., Gerber, C., Joss, A., Haenni, S., Meier, A., Hashorva, E., & Lang, N. P. (2004). Patterns of tissue remodeling after placement of ITI dental implants using an osteotome technique: A longitudinal radiographic case cohort study. *Clinical Oral Implants Research*, *15*, 158–166.

Buser, D., Weber, H. P., & Lang, N. P. (1990). Tissue integration of non-submerged implants. 1-year results of a prospective study with 100 ITI hollow-cylinder and hollow-screw implants. *Clinical Oral Implants Research*, *1*, 33–40.

Cardoso, R. G., Melo, L. A. d., Barbosa, G. A. S., Calderon, P. D. S., Germano, A. R., Mestriner, W., & Carreiro, A. d. F. P. (2016). Impact of mandibular conventional denture and overdenture on quality of life and masticatory efficiency. *Brazilian Oral Research*, *30*, e102.

Cho-Yan Lee, J., Mattheos, N., Nixon, K. C., & Ivanovski, S. (2012). Residual periodontal pockets are a risk indicator for peri-implantitis in patients treated for periodontitis. *Clinical Oral Implants Research*, *23*, 325–333.

Derks, J., Håkansson, J., Wennström, J. L., Tomasi, C., Larsson, M., & Berglundh, T. (2015). Effectiveness of implant therapy analyzed in a Swedish population: Early and late implant loss. *Journal of Dental Research*, *94*, 44S–51S.

Derks, J., Schaller, D., Håkansson, J., Wennström, J. L., Tomasi, C., & Berglundh, T. (2016). Effectiveness of implant therapy analyzed in a Swedish population: Prevalence of peri-implantitis. *Journal of Dental Research*, *95*, 43–49.

El-Sheikh, A. M., Shihabuddin, O. F., & Ghoraba, S. M. F. (2012). Two versus three narrow-diameter implants with locator attachments supporting mandibular overdentures: A two-year prospective study. *International Journal of Dentistry*, *2012*, 285684.

Engfors, I., Ortorp, A., & Jemt, T. (2004). Fixed implant-supported prostheses in elderly patients: A 5-year retrospective study of 133 edentulous patients older than 79 years. *Clinical Implant Dentistry and Related Research*, *6*, 190–198.

Enkling, N., Saftig, M., Worni, A., Mericske-Stern, R., & Schimmel, M. (2017). Chewing efficiency, bite force and oral health-related quality of life with narrow diameter implants – a prospective clinical study: Results after one year. *Clinical Oral Implants Research*, *28*, 476–482.

Feine, J. S., Carlsson, G. E., Awad, M. A., Chehade, A., Duncan, W. J., Gizani, S., Head, T., Heydecke, G., Lund, J. P., MacEntee, M., Mericske-Stern, R., Mojon, P., Morais, J. A., Naert, I., Payne, A. G. T., Penrod, J., Stoker, G. T., Tawse-Smith, A., Taylor, T. D., … Wismeijer, D. (2002). The McGill consensus statement on overdentures. Mandibular two-implant overdentures as first choice standard of care for edentulous patients. *Gerodontology*, *19*, 3–4.

Fernandes, P. R. E., Otero, A. I. P., Fernandes, J. C. H., Nassani, L. M., Castilho, R. M., & de Oliveira Fernandes, G. V. (2022). Clinical performance comparing titanium and titanium–zirconium or zirconia dental implants: A systematic review of randomized controlled trials. *Dentistry Journal*, *10*, 83.

Galli, S., Jimbo, R., Naito, Y., Berner, S., Dard, M., & Wennerberg, A. (2017). Chemically modified titanium–zirconium implants in comparison with commercially pure titanium controls stimulate the early molecular pathways of bone healing. *Clinical Oral Implants Research*, *28*, 1234–1240.

Ghazal, S. S., Huynh-Ba, G., Aghaloo, T., Dibart, S., Froum, S., O'Neal, R., & Cochran, D. (2019). A randomized, controlled, multicenter clinical study evaluating the crestal bone level change of SLActive bone level Ø 3.3 mm implants compared to SLActive bone level Ø 4.1 mm implants for single-tooth replacement. *The International Journal of Oral & Maxillofacial Implants*, *34*, 708–718.

Gruica, B., Wang, H.-Y., Lang, N. P., & Buser, D. (2004). Impact of IL-1 genotype and smoking status on the prognosis of osseointegrated implants. *Clinical Oral Implants Research*, *15*, 393–400.

Hof, M., Tepper, G., Semo, B., Arnhart, C., Watzek, G., & Pommer, B. (2014). Patients' perspectives on dental implant and bone graft surgery: Questionnaire-based interview survey. *Clinical Oral Implants Research*, *25*, 42–45.

Hotchkiss, K. M., Ayad, N. B., Hyzy, S. L., Boyan, B. D., & Olivares-Navarrete, R. (2017). Dental implant surface chemistry and energy alter macrophage activation *in vitro*. *Clinical Oral Implants Research*, *28*, 414–423.

Hotchkiss, K. M., Sowers, K. T., & Olivares-Navarrete, R. (2019). Novel in vitro comparative model of osteogenic and inflammatory cell response to dental implants. *Dental Materials*, *35*, 176–184.

Hugoson, A., Koch, G., Göthberg, C., Helkimo, A. N., Lundin, S.-A., Norderyd, O., Sjödin, B., & Sondell, K. (2005). Oral health of individuals aged 3–80 years in Jönköping, Sweden during 30 years (1973–2003). II. Review of clinical and radiographic findings. *Swedish Dental Journal*, *29*, 139–155.

Hultin, K., Eriksson, A., Backe, C., Johansson, U., & Bougas, K. (2020). A pilot study with randomised controlled design comparing TiZr alloy dental implants to Ti implants. *Journal of Oral and Maxillofacial Research*, *11*, e3.

Jepsen, S., Berglundh, T., Genco, R., Aass, A. M., Demirel, K., Derks, J., Figuero, E., Giovannoli, J. L., Goldstein, M., Lambert, F., Ortiz-Vigon, A., Polyzois, I., Salvi, G. E., Schwarz, F., Serino, G., Tomasi, C., & Zitzmann, N. U. (2015). Primary prevention of peri-implantitis: Managing peri-implant mucositis. *Journal of Clinical Periodontology*, *42*(Suppl 16), S152–S157.

Jimbo, R., Naito, Y., Galli, S., Berner, S., Dard, M., & Wennerberg, A. (2015). Biomechanical and histomorphometrical evaluation of TiZr alloy implants: An in vivo study in the rabbit: Osseointegration property of TiZr alloy implants. *Clinical Implant Dentistry and Related Research*, *17*, e670–e678.

Kämmerer, P. W., Palarie, V., Schiegnitz, E., Hagmann, S., Alshihri, A., & Al-Nawas, B. (2014). Vertical osteoconductivity and early bone formation of titanium–zirconium and titanium implants in a subperiosteal rabbit animal model. *Clinical Oral Implants Research*, *25*, 774–780.

Kobayashi, E., Matsumoto, S., Doi, H., Yoneyama, T., & Hamanaka, H. (1995). Mechanical properties of the binary titanium–zirconium alloys and their potential for biomedical materials. *Journal of Biomedical Materials Research*, *29*, 943–950.

Kowar, J., Eriksson, A., & Jemt, T. (2013). Fixed implant-supported prostheses in elderly patients: A 5-year retrospective comparison between partially and completely edentulous patients aged 80 years or older at implant surgery. *Clinical Implant Dentistry and Related Research*, *15*, 37–46.

Kremer, U., Schindler, S., Enkling, N., Worni, A., Katsoulis, J., & Mericske-Stern, R. (2016). Bone resorption in different parts of the mandible in patients restored with an implant overdenture. A retrospective radiographic analysis. *Clinical Oral Implants Research*, *27*, 267–272.

Kutkut, A., Bertoli, E., Frazer, R., Pinto-Sinai, G., Fuentealba Hidalgo, R., & Studts, J. (2018). A systematic review of studies comparing conventional complete denture and implant retained overdenture. *Journal of Prosthodontic Research*, *62*, 1–9.

LaBarre, E. E., Ahlstrom, R. H., & Noble, W. H. (2008). Narrow diameter implants for mandibular denture retention. *Journal of the California Dental Association*, *36*, 283–286.

Laurell, L., & Lundgren, D. (2011). Marginal bone level changes at dental implants after 5 years in function: A meta-analysis: Marginal bone level changes at dental implants. *Clinical Implant Dentistry and Related Research*, *13*, 19–28.

Lesaffre, E., Garcia Zattera, M.-J., Redmond, C., Huber, H., Needleman, I., & ISCB Subcommittee on Dentistry. (2007). Reported methodological quality of split-mouth studies. *Journal of Clinical Periodontology*, *34*, 756–761.

Marcello-Machado, R. M., Faot, F., Schuster, A. J., Nascimento, G. G., & Del Bel Cury, A. A. (2018). Mini-implants and narrow diameter implants as mandibular overdenture retainers: A systematic review and meta-analysis of clinical and radiographic outcomes. *Journal of Oral Rehabilitation*, *45*, 161–183.

Mombelli, A., van Oosten, M. A., Schürch, E. Jr, & Lang, N. P. (1987). The microbiota associated with successful or failing osseointegrated titanium implants. *Oral Microbiology and Immunology*, *2*(4), 145–151.

Müller, F. (2014). Interventions for edentate elders – what is the evidence? *Gerodontology*, *31*(Suppl 1), 44–51.

Müller, F., Al-Nawas, B., Storelli, S., Quirynen, M., Hicklin, S., Castro-Laza, J., Bassetti, R., & Schimmel, M. (2015). Small-diameter titanium grade IV and titanium–zirconium implants in edentulous mandibles: Five-year results from a double-blind, randomized controlled trial. *BMC Oral Health*, *15*, 123.

Müller, F., Duvernay, E., Loup, A., Vazquez, L., Herrmann, F. R., & Schimmel, M. (2013). Implant-supported mandibular overdentures in very old adults: A randomized controlled trial. *Journal of Dental Research*, *92*, 154S–160S.

Müller, F., Hernandez, M., Grütter, L., Aracil-Kessler, L., Weingart, D., & Schimmel, M. (2012). Masseter muscle thickness, chewing efficiency and bite force in edentulous patients with fixed and removable implant-supported prostheses: A cross-sectional multicenter study. *Clinical Oral Implants Research*, *23*, 144–150.

Müller, F., Wahl, G., & Fuhr, K. (1994). Age-related satisfaction with complete dentures, desire for improvement and attitudes to implant treatment. *Gerodontology*, *11*, 7–12.

Norderyd, O., Koch, G., Papias, A., Köhler, A. A., Helkimo, A. N., Brahm, C.-O., Lindmark, U., Lindfors, N., Mattsson, A., Rolander, B., Ullbro, C., Gerdin, E. W., & Frisk, F. (2015). Oral health of individuals aged 3-80 years in Jönköping, Sweden during 40 years (1973-2013). II. Review of clinical and radiographic findings. *Swedish Dental Journal*, *39*, 69–86.

Øzhayat, E. B., & Gotfredsen, K. (2019). Patient-reported effect of oral rehabilitation. *Journal of Oral Rehabilitation*, *46*, 369–376.

Papaspyridakos, P., Chen, C.-J., Chuang, S.-K., & Weber, H.-P. (2014). Implant loading protocols for edentulous patients with fixed prostheses: A systematic review and meta-analysis. *The International Journal of Oral & Maxillofacial Implants*, *29*, 256–270.

Patzelt, S. B. M., Bahat, O., Reynolds, M. A., & Strub, J. R. (2014). The all-on-four treatment concept: A systematic review: All-on-4. *Clinical Implant Dentistry and Related Research*, *16*, 836–855.

Pommer, B., Mailath-Pokorny, G., Haas, R., Busenlechner, D., Fürhauser, R., & Watzek, G. (2014). Patients' preferences towards minimally invasive treatment alternatives for implant rehabilitation of edentulous jaws. *European Journal of Oral Implantology*, *7*(Suppl 2), S91–S109.

Quirynen, M., Al-Nawas, B., Meijer, H. J. A., Razavi, A., Reichert, T. E., Schimmel, M., Storelli, S., Romeo, E., & Roxolid Study Group. (2015). Small-diameter titanium grade IV and titanium–zirconium implants in edentulous mandibles: Three-year results from a double-blind, randomized controlled trial. *Clinical Oral Implants Research*, *26*, 831–840.

Rashid, F., Awad, M. A., Thomason, J. M., Piovano, A., Spielberg, G. P., Scilingo, E., Mojon, P., Müller, F., Spielberg, M., Heydecke, G., Stoker, G., Wismeijer, D., Allen, F., & Feine, J. S. (2011). The effectiveness of 2-implant overdentures – a pragmatic international multicentre study. *Journal of Oral Rehabilitation*, *38*, 176–184.

Riemann, M., Wachtel, H., Beuer, F., Bolz, W., Schuh, P., Niedermaier, R., & Stelzle, F. (2019). Biologic and technical complications of implant-supported immediately loaded fixed full-arch prostheses: An evaluation of up to 6 years. *The International Journal of Oral & Maxillofacial Implants*, *34*, 1482–1492.

Salvi, G. E., Cosgarea, R., & Sculean, A. (2017). Prevalence and mechanisms of peri-implant diseases. *Journal of Dental Research*, *96*, 31–37.

Saulacic, N., Bosshardt, D. D., Bornstein, M. M., Berner, S., & Buser, D. (2012). Bone apposition to a titanium–zirconium alloy implant, as compared to two other titanium-containing implants. *European Cells & Materials*, *23*, 273–286. discussion 286-288.

Schimmel, M., Müller, F., Suter, V., & Buser, D. (2017). Implants for elderly patients. *Periodontology*, *2000*(73), 228–240.

Schimmel, M., Srinivasan, M., Herrmann, F. R., & Müller, F. (2014). Loading protocols for implant-supported overdentures in the edentulous jaw: A systematic review and meta-analysis. *The International Journal of Oral & Maxillofacial Implants*, *29*(Suppl), 271–286.

Sohrabi, K., Mushantat, A., Esfandiari, S., & Feine, J. (2012). How successful are small-diameter implants? A literature review. *Clinical Oral Implants Research*, *23*, 515–525.

Srinivasan, M., Kamnoedboon, P., Angst, L., & Müller, F. (2023). Oral function in completely edentulous patients rehabilitated with implant-supported dental prostheses: A systematic review and meta-analysis. *Clinical Oral Implants Research*, *34*, 196–239.

Steele, J. G., Sanders, A. E., Slade, G. D., Allen, P. F., Lahti, S., Nuttall, N., & Spencer, A. J. (2004). How do age and tooth loss affect oral health impacts and quality of life? A study comparing two national samples. *Community Dentistry and Oral Epidemiology*, *32*, 107–114.

Thoma, D. S., Jones, A. A., Dard, M., Grize, L., Obrecht, M., & Cochran, D. L. (2011). Tissue integration of a new titanium–zirconium dental implant: A comparative histologic and radiographic study in the canine. *Journal of Periodontology*, *82*, 1453–1461.

Thomason, J. M., Kelly, S. a. M., Bendkowski, A., & Ellis, J. S. (2012). Two implant retained overdentures—a review of the literature supporting the McGill and York consensus statements. *Journal of Dentistry*, *40*, 22–34.

Ueda, T., Kremer, U., Katsoulis, J., & Mericske-Stern, R. (2011). Long-term results of mandibular implants supporting an overdenture: Implant

survival, failures, and crestal bone level changes. *The International Journal of Oral & Maxillofacial Implants*, *26*, 365–372.

Van Der Bilt, A., Burgers, M., Van Kampen, F. M. C., & Cune, M. S. (2010). Mandibular implant-supported overdentures and oral function: Overdentures and oral function. *Clinical Oral Implants Research*, *21*, 1209–1213.

Vogel, R., Smith-Palmer, J., & Valentine, W. (2013). Evaluating the health economic implications and cost-effectiveness of dental implants: A literature review. *The International Journal of Oral & Maxillofacial Implants*, *28*, 343–356.

Walton, J. N., & MacEntee, M. I. (2005). Choosing or refusing oral implants: A prospective study of edentulous volunteers for a clinical trial. *The International Journal of Prosthodontics*, *18*, 483–488.

Wen, B., Zhu, F., Li, Z., Zhang, P., Lin, X., & Dard, M. (2014). The osseointegration behavior of titanium–zirconium implants in ovariectomized rabbits. *Clinical Oral Implants Research*, *25*, 819–825.

Yunus, N., Masood, M., Saub, R., Al-Hashedi, A. A., Taiyeb Ali, T. B., & Thomason, J. M. (2016). Impact of mandibular implant prostheses on the oral health-related quality of life in partially and completely edentulous patients. *Clinical Oral Implants Research*, *27*, 904–909.

Zangrando, M. S., Damante, C. A., Sant'Ana, A. C., Rubo de Rezende, M. L., Greghi, S. L., & Chambrone, L. (2015). Long-term evaluation of periodontal parameters and implant outcomes in periodontally compromised patients: A systematic review. *Journal of Periodontology*, *86*, 201–221.

Zhang, L., Lyu, C., Shang, Z., Niu, A., & Liang, X. (2017). Quality of life of implant-supported overdenture and conventional complete denture in restoring the edentulous mandible: A systematic review. *Implant Dentistry*, *26*, 945–950.

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APPENDIX

On behalf of the Roxolid Study Group

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