Table 3. Summary of RCT on periodontal regeneration with mesenchymal stem cells

Author	Study design	Cell type	Stem cells handling	Defect type	Number of patients	Treatment groups	Follow-up	Outcome variables	Results
Akbay *et al*.[112] 2005	RCT with a split mouth design	PDLSC	Direct application of PDL tissue collected from an extracted molar, into the defect	Class II mandibular furcation defects	10 patients 20 defects: 10test/10 control	Test: coronally positioned flap with autogenous PDL grafts that were obtained from third molars Control: coronally positioned flap alone	6 months, with a surgical re-entry	Clinical: PI, GI, PD, GR, CAL Radiographic: linear and volumetric evaluation Volumetric defect fill by impression of the defects Histologic analysis by gingival biopsy from one patient	Sites treated with PDL grafts demonstrated significant improvement in vertical and horizontal defect fill, PD, and CAL at 3 and 6 months compared to pre-surgical values. The difference determined for the PD values of both groups at a statistically significant degree in favor of grafted sites was maintained at all observation periods. No foreign body reaction was observed in PDL grafts
Chen *et al*.[120] 2016	single-center RCT	PDLSC	Collection from an extracted molar, isolation, culture, characterization and engineering into cells sheets in laboratory	Intrabony defects	30 patients 41 defects: 20 test/21 control	Test: GTR and PDLSC sheets in combination with demineralized bovine bone matrix Control: GTR and demineralized bovine bone matrix without stem cells	12 months	Radiographic (main outcome): Increase in alveolar bone height (rx bone fill) Clinical: CAL, PPD, REC Safety assessment: blood and urine examination	Both groups showed a significant increase in the alveolar bone height, without statistically significant differences between groups. Regarding the clinical periodontal parameters, no statistically significant differences were found for the increased CAL, PD or GR between the cell and control groups. No adverse effects on the use of PDL cells sheets were reported
Dhote *et al*.[123] 2015	Parallel designed RCT	UC-MSC	Collection from the hospital in a sterile tube Followed by isolation and culture on β-TCP scaffold	Intrabony defects	14 patients 24 defects: 12 test/ 12 control	Test: ODF applying allogeneic UC-MSCs on a β-TCP scaffold in combination rh-PDGF-BB Control: OFD	6 months	Clinical: PI, BPI, CAL, PPD, relative gingival marginal level Radiographic: linear bone growth (LBG)	The test protocol resulted in a significant added benefit in terms of CAL gains, PPD reductions greater radiographic defect fill and improvement in Linear bone growth compared to the OFD alone. No adverse effects, allergy, infection or patients complaints related to the graft material were reported
Ferrarotti *et al*.[122] 2018	Parallel, double-blind, prospective RCT	DPSC	Mechanical dissociation of the dental pulp of an extracted tooth by the use of a biological tissue disaggregator to obtain micrografts rich in autologous DPSC endorsed on a collagen sponge	Intrabony defects	29 patients 29 defects: 15 test/14 control	Test: minimally invasive surgical technique (MIST) plus dental pulp micrografts in a collagen sponge biocomplex Control: MIST plus collagen sponge alone	12 months	Clinical: PI, Bop, PD, REC, CAL Radiographic: bone fill	Test sites exhibited significantly more PD reduction, CAL gain and bone defect fill than controls. Moreover, residual PD < 5 mm and CAL gain ≥ 4 mm were significantly more frequent in the test group. No adverse effects were reported