Efficacy and safety of a fibrin sealant for adherence of autologous skin grafts to burn wounds: Results of a phase 3 clinical study.

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Abstract:

The objective of this phase 3, multicentered, prospective, randomized, evaluator-blinded, clinical study was to compare skin graft adherence utilizing a fibrin sealant containing 4 IU/ml thrombin (FS 4IU VH S/D [FS 4IU VH S/D will be marketed under the trade name ARTISS upon licensure in the United States]) to graft adherence utilizing staples in burn patients requiring wound excision and skin grafting. FS 4IU VH S/D was compared with staples in 138 patients. Patients had burn wounds measuring <=40% of total body surface area with two comparable test sites measuring between 1 and 4% total body surface area each. Wound closure at day 28 was assessed using test site planimetry and review of day 28 photographs by three independent blinded evaluators (primary endpoint analysis). Secondary efficacy measures included hematoma/seroma on day 1, engraftment on day 5, and wound closure on day 14. Investigator and patient-reported outcomes were also assessed. The proportion of test sites with complete wound closure at day 28 was 70.3% in FS 4IU VH S/D treated sites and 65.8% in stapled sites, as assessed by planimetry. Blinded review of day 28 photographs confirmed that the rate of complete wound closure was similar between the two treatments, although the overall assessed rates of closure were lower than those determined by planimetry: FS 4IU VH S/D (43.3%) and staples (37.0%). The lower limit of the 97.5% confidence interval of the difference between FS 4IU VH S/D and staples was -0.029, which is above the predefined noninferiority margin of -0.1. Therefore, FS 4IU VH S/D is at least as efficacious as

staples at the 97.5% one-sided level for complete wound closure by day 28. Hematoma/seroma on day 1 occurred at significantly (P < .0001) fewer FS 4IU VH S/D-treated sites (29.7% [95% CI 22.2-38.1%]) compared with stapled sites (62.3% [95% CI 53.7-70.4%]). Engraftment on day 5 was deemed to be 100% in 62.3% (95% CI 53.7-70.4%) of the FS 4IU VH S/D-treated sites and 55.1% (95% CI 46.4-63.5%) of the stapled sites (P = .0890). Complete wound closure by day 14 occurred in 48.8% (95% CI 39.9-57.8%) of the FS 4IU VH S/D treated sites and 42.6% (95% CI 34.0-51.6%) of the stapled sites (P = .2299). FS 4IU VH S/D scored significantly better than staples for all investigator-assessed outcomes, namely quality of graft adherence (P < .0001), preference for method of fixation (P < .0001), satisfaction with graft fixation (P < .0001), and overall quality of healing (P < .0001). Likewise, FS 4IU VH S/D scored significantly better than staples for all patient-assessed outcomes, namely anxiety about pain (P < .0001) and treatment preference (P <.0001). The safety profile of FS 4IU VH S/D was excellent as indicated by the lack of any related serious adverse experiences. These findings demonstrate that FS 4IU VH S/D is safe and effective for attachment of skin grafts, with outcomes at least as good as or better than staple fixation.