

5.3.8.1 Primary Efficacy Measurements

(Content from P060021/A011, November 2007 Amendment, Section V, Clinical, Section 4.1, Pages 41-42)

5.3.8.1 Primary Efficacy Measurements – Overall Success**Overall Success at 24 months (with 36+ month retreatment and radiographic data) from Pivotal Study S01-01US/Extension Study 06-UPLF-01**

The primary efficacy endpoint is the Overall Success rate for the mITT population, in which missing data were imputed. Overall success is a composite endpoint consisting of radiographic success, improvement in Oswestry Disability Index, absence of retreatment, absence of neurological compromise, and absence of serious treatment-related adverse events. Success regarding the improvement of ODI, absence of neurological compromise, and absence of serious treatment-related adverse events is determined at 24 months from the data collected in the original pivotal study, S01-01US. Success regarding radiographic evidence of fusion (presence of bone by CT scan, angular motion success and translational movement success by plain films) is based on the 36+ months data collected in this study. Results for the primary endpoint of Overall Success and for the subcomponents of Overall Success are presented in Table 10.

Table 10: Overall Success at 24 months (with Radiographic and Retreatment subcomponents at 36+ months) mITT Population

Outcome	OP-1 Putty		Autograft		p-value Non-inferiority
	Number of Patients	N (%) Successes	Number of Patients	N (%) Successes	
Overall Success ^{1,2}	207	97.75 (47.2)	86	40.25 (46.8)	0.025 ²

¹ Missing values were imputed.

² p-value is based on one-sided 2-sample test for non-inferiority in the angular scale with a non-inferiority margin of 0.14 (radians); estimates and standard errors are based on logistic regression and multiple imputation.

In this analysis using retreatment and radiographic data collected at the 36+ month interval (where presence of bone was assessed using CT scan rather than plain films), OP-1 Putty demonstrated non-inferiority to autograft with regard to the pre-specified primary composite endpoint Overall Success. OP-1 Putty achieved 47.2% success and autograft achieved 46.8% success (p=0.025).