

### **5.3.7 Demographics and Baseline Characteristics**

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### **DEMOGRAPHICS**

#### **Baseline Demographics for S01-01US**

Table 7 presents demographics and baseline characteristics by treatment group and overall for the S01-01US mITT population. No statistically significant differences between treatment groups were noted. (Further discussion of demographics is presented in section 1.2 of clinical study report CSR S01-01US in Appendix B of Section V of the original PMA submission.)

#### *Age and Gender*

Overall mean age was 68 years, with the range among groups of 36 to 84 years. The groups were similar in age distribution, with a majority of patients in each group aged >65 years.

Approximately two-thirds of the patients were women, which is expected because the diagnosis of degenerative spondylolisthesis<sup>16</sup> is more prevalent in women.

#### *Weight and Height*

Weight and height were similar across both treatment groups.

#### *Diagnosis*

Ninety-three percent of patients in the OP-1 Putty group and 92% of patients in the autograft group had lumbar spinal stenosis with a definitive diagnosis of Grade 1 degenerative lumbar spondylolisthesis.

#### *Treated Level*

Eighty-six percent of patients in both treatment groups had disease involvement at the L4-L5 level.

#### *Disease Severity Indices*

The ODI and measurements of degree of angular motion and translational movement were assessed at baseline and at specified time points throughout the study period. There were no statistically significant differences between groups.

#### *Method Used to Determine Diagnosis*

Statistical Table 2.2 in Section 14 presents methods used to determine diagnosis. Greater than 90% of patients in both treatment groups were diagnosed via AP radiograph, lateral radiograph, flexion/extension radiograph and/or MRI.

#### *Prior Treatments to Affect Level*

Statistical Table 2.2 in Section 14 presents prior treatment history. Overall the most commonly used treatment modalities used by patients prior to study enrollment included non-steroidal medication (75.1%), physical therapy (72.4%), and systemic and local steroid administration (58.0%). Treatment histories were balanced between the two groups.

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*Worker's Compensation Status*

Statistical Table 2.2 in Section 14 presents worker's compensation status. Fewer than 4% of patients were currently on worker's compensation.

**Table 7: Selected Demographic and Baseline Characteristics (Modified ITT Population), S01-01US**

Parameter	Statistic	Overall	OP-1 Putty	Autograft	P Value <sup>a</sup>	
Age (years)	N	293	207	86	0.129	
	Mean	68	68	69		
	Median	69	68	71		
	Std. Dev.	9.4	9.8	8.3		
Sex: Male	N (%)	97 (33.1)	71 (34.3)	26 (30.2)	0.501	
	Female	N (%)	196 (66.9)	136 (65.7)		60 (69.8)
Weight (kg)	N	292	206	86	0.200	
	Mean	79.6	78.8	81.5		
	Median	79.4	78.1	82.4		
	Std. Dev.	16.32	16.06	16.88		
Height (cm)	N	293	207	86	0.268	
	Mean	165.8	165.4	166.8		
	Median	165.1	165.0	165.8		
	Std. Dev.	9.53	9.25	10.17		
Level Fused <sup>b</sup> :	L3-L4	n (%)	31 (10.6)	21 (10.1)	10 (11.6)	0.760
	L4-L5	n (%)	252 (86.0)	178 (86.0)	74 (86.0)	
	L5-S1	n (%)	10 (3.4)	8 (3.9)	2 (2.3)	
ODI	n	293	207	86	0.998	
	Mean	48.8	48.8	48.8		
	Median	48.0	48.9	48.0		
	Std. Dev.	12.19	11.60	13.59		
Degree of Angular Motion <sup>c</sup> (degrees)	n	271	195	76	0.086	
	Mean	4.1	3.9	4.7		
	Median	3.1	2.8	4.2		
	Std. Dev.	3.36	3.40	3.20		
Translational Movement <sup>c</sup> (mm)	n	268	193	75	0.802	
	Mean	1.7	1.7	1.6		
	Median	1.4	1.4	1.1		
	Std. Dev.	1.45	1.44	1.49		
Diagnosis of degenerative lumbar spondylolisthesis with spinal stenosis	n (%)	293 (100.0)	207 (100.0)	86 (100.0)	---	
	Grade 1	n (%)	272 (92.8)	193 (93.2)		79 (91.9)
	Grade 2	n (%)	10 (3.4)	8 (3.9)		2 (2.3)
	Unable to distinguish between Grade 1 and 2	n (%)	11 (3.8)	6 (2.9)		5 (5.8)

Note: Percentages are based on total number of patients for each treatment group or overall as appropriate.

(a) P Value is based on Chi-Square test for the categorical variables, and is based on 2-sample *t* test for the continuous variables.

(b) Subject 3101 had involved level L5-S1 different from level fused L3-L4.

(c) The average scores from the 2 reviewers were used in the analysis.

Source: Section 11.2 of CSR S01-01US in Appendix B of Section V of original PMA submission.

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#### Demographics for Patients Eligible for 06-UPLF-01 Versus Patients Who Returned for 06-UPLF-01

Of all S01-01US study patients eligible for participation in 06-UPLF-01 (n=257, 183 for OP-1 Putty group and 74 for autograft group), the key demographics and baseline characteristics and key success outcomes (at 24 months as measured in S01-01US) between treatment groups for the patients who enrolled in 06-UPLF-01 versus the patients who were eligible for 06-UPLF-01 have been maintained.

The S01-01US population that was eligible to participate in 06-UPLF-01 (had not been a retreatment failure in S01-01US and had not died) can be characterized as elderly (mean age at surgery of 67.6 for OP-1 and 69.3 for autograft), more females than males (65.0% for OP-1 Putty and 74.3% for autograft), with comparable mean weights (78.9kg for OP-1 Putty and 80.6kg for autograft), comparable mean heights (165.5cm for OP-1 Putty and 165.8 for autograft), similar mean pre-operative ODI scores (48.5 for OP-1 Putty and 50.1 for autograft), similar mean pre-operative angular motion (4.0° for OP-1 Putty and 4.7° for autograft), and similar mean pre-operative translational movement (1.7mm for OP-1 Putty and 1.6mm for autograft). Although spondylolisthesis of Grade 1 or Grade 2 with spinal stenosis was permitted in the study, both groups featured predominantly Grade 1 spondylolisthesis (92.3% Grade 1 for OP-1 Putty and 91.9% Grade 1 for autograft population). Almost all patients were not on Worker's Compensation (95.1% for OP-1 Putty and 98.6% for autograft). In addition to comparing baseline demographic characteristics, it should be noted that the percent of patients eligible for 06-UPLF-01 who had achieved Overall Success at 24 months as originally defined in pivotal study S01-01US (using assessment of fusion by plain films at 24 months) was 42.9% for the OP-1 Putty group and 57.6% for the autograft group (Source: Statistical Table S.2 in Section 14.1 of CSR 06-UPLF-01, Appendix B to section V of this PMA Amendment), which does not reflect a difference in baseline characteristics, but rather reflects the higher success rate achieved in the autograft group at 24 months using the original Overall Success definition in S01-01US. For those patients who returned for evaluation under protocol 06-UPLF-01, demographics between the OP-1 Putty group and the autograft group continue to be comparable to each other as well as to the corresponding groups for the entire population that was eligible to participate in 06-UPLF-01. The patients who returned for evaluation under 06-UPLF-01 can also be characterized as elderly (mean age at surgery of 66.8 for OP-1 and 68.7 for autograft), more females than males (65.3% for OP-1 Putty and 72.4% for autograft), with comparable mean weights (79.0kg for OP-1 Putty and 81.0kg for autograft), comparable mean heights (165.9cm for OP-1 Putty and 166.1cm for autograft), similar mean pre-operative ODI scores (48.2 for OP-1 Putty and 50.7 for autograft), similar mean pre-operative angular motion (4.1° for OP-1 Putty and 4.3° for autograft), and similar mean pre-operative translational movement (1.8mm for OP-1 Putty and 1.5mm for autograft). Both study groups featured predominantly Grade 1 spondylolisthesis (93.8% Grade 1 for OP-1 Putty and 93.1% Grade 1 for autograft population). As with the original Pivotal IDE population, nearly all patients were not on Worker's Compensation: 95.8% for OP-1 Putty and 98.3% for autograft. The percent of patients who had achieved Overall Success at 24 months as originally defined in pivotal study S01-01US (using assessment of fusion by plain films at 24 months) was 43.8% for the OP-1 Putty group and 60.0% for the autograft group, which is consistent with the overall success rates at 24 months for each treatment group in the entire population eligible to return for 06-UPLF-01. (Source:

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Statistical Table S.2 in Section 14.1 of CSR 06-UPLF-01 in Appendix B to section V of this PMA Amendment.)

Table 8 presents a comparison of demographic and baseline characteristics by treatment group between the population eligible for 06-UPLF-01 and the population who actually returned to participate in extension study 06-UPLF-01. The comparison demonstrates that there were no apparent differences in key characteristics, thus providing reasonable assurance that the results of the 36+ month analyses are representative of the entire study population, and that the extension study does not appear to have introduced a source of bias by disproportionately representing those patients pre-disposed to success or failure.

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**Table 8: Summary of Key Demographic Parameters for Pivotal IDE S01-01US and Extension Study 06-UPLF-06**

Parameter	Statistic	OP-1 Putty		Autograft	
		Eligible for 06-UPLF-01	Enrolled in 06-UPLF-01	Eligible for 06-UPLF-01	Enrolled in 06-UPLF-01
Age (years)	N	183	144	74	58
	Mean	67.6	66.8	69.3	68.7
	Median	69.0	67.0	71.0	70.0
	Std. Dev.	9.54	9.25	8.72	8.66
Sex: Male	N (%)	64 (35.0)	50 (34.7)	19 (25.7)	16 (27.6)
	Female	N (%)	119 (65.0)	94 (65.3)	55 (74.3)
Weight (kg)	N	183	144	74	58

Parameter	Statistic	OP-1 Putty		Autograft		
		Eligible for 06-UPLF-01	Enrolled in 06-UPLF-01	Eligible for 06-UPLF-01	Enrolled in 06-UPLF-01	
	Mean	78.9	79.0	80.6	81.0	
	Median	79.4	79.4	81.6	82.4	
	Std. Dev.	16.08	15.71	17.41	17.98	
Height (cm)	n	183	144	74	58	
	Mean	165.5	165.9	165.8	166.1	
	Median	165.1	165.1	165.1	165.1	
	Std. Dev.	9.26	9.18	10.20	9.36	
Level Fused:	L3-L4	n (%)	19 (10.4)	17 (11.8)	10 (13.5)	9 (15.5)
	L4-L5	n (%)	156 (85.2)	124 (86.1)	62 (83.8)	48 (82.8)
	L5-S1	n (%)	8 (4.4)	3 (2.1)	2 (2.7)	1 (1.7)
ODI	n	183	144	74	58	
	Mean	48.5	48.2	50.1	50.7	
	Median	48.9	48.9	48.0	48.0	
	Std. Dev.	11.11	10.74	13.48	12.47	
Degree of Angular Motion <sup>b</sup> (degrees)	n	174	138	66	51	
	Mean	4.0	4.1	4.7	4.3	
	Median	2.8	2.9	4.1	3.6	
	Std. Dev.	3.42	3.53	3.24	3.03	
Translational Movement <sup>b</sup> (mm)	n	171	136	65	51	
	Mean	1.7	1.8	1.6	1.5	
	Median	1.4	1.5	1.0	0.8	
	Std. Dev.	1.48	1.55	1.52	1.42	
Diagnosis of degenerative lumbar spondylolisthesis with spinal stenosis	n (%)	183 (100)	144 (100)	74 (100)	58 (100)	
Grade 1	n (%)	169 (92.3)	135 (93.8)	68 (91.9)	54 (93.1)	
Grade 2	n (%)	8 (4.4)	5 (3.5)	2 (2.7)	2 (3.4)	
Unable to distinguish between Grade 1 and 2	n (%)	6 (3.3)	4 (2.8)	4 (5.4)	2 (3.4)	
Prior overall success at 24 months as determined in pivotal study S01-01US	%	42.9	43.8	57.6	60.0	
Prior success in presence of bone assessment by 9 month CT scan in pivotal study S01-01US	%	91.2	89.7	98.4	100.0	

(a) Subject 3101 in S01-01US had involved level L5-S1 different from level fused L3-L4.

(b) This represents the average scores from the 2 reviewers used in the analysis for pivotal study S01-01US. Source: Statistical Table S.1.4 and S.2 in Section 14.1 of CSR 06-UPLF-01, Appendix B to section V of this PMA Amendment