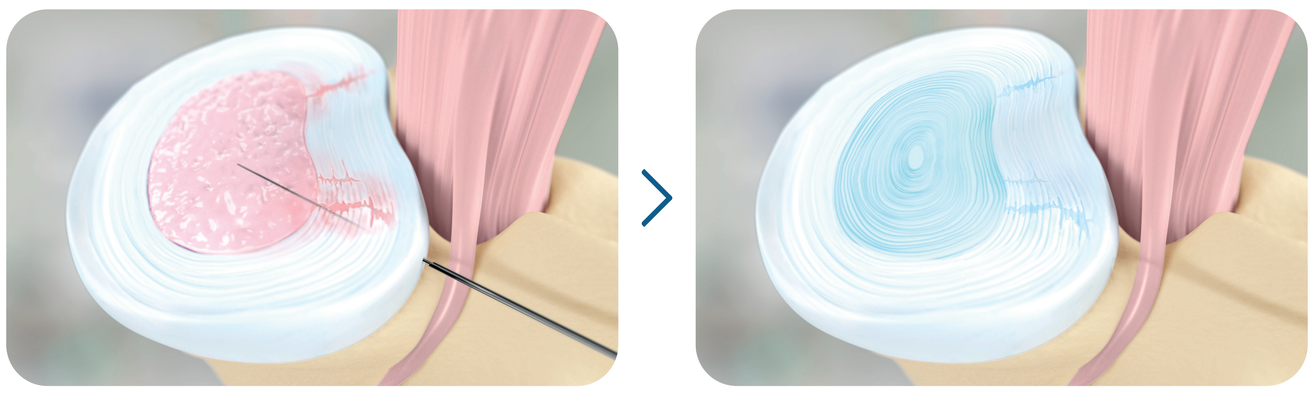
SAFETY AND TOLERABILITY OF STA363 IN PATIENTS WITH DEGENERATIVE DISC DISEASE: INTERIMISTIC DATA FROM A PHASE 2B STUDY

Anders Lehmann[1], Andreas Gerward[1], Björn Strömqvist[2], Douglas Beall[3]
[1]Stayble Therapeutics, Gothenburg, Sweden | [2]Department of Orthopedics, University Hospital Malmö/Lund, Sweden | [3]Interventional Radiology, Comprehensive Specialty Care, Oklahoma City, OK, USA

INTRODUCTION

Transformation of the nucleus pulposus into fibrotic tissue may increase flexural rigidity and decrease inflammation of the painful degenerated intervertebral disc. Intradiscal STA363 (lactic acid) has been shown to effectively induce fibrosis in pigs and MRI data from a phase 1b study[1] suggest that a similar effect occurs in patients suffering from degenerative disc disease (DDD, Fig. 1). In an ongoing, fully recruited, double-blind, randomised phase 2b study, the primary objective is to determine the effect of STA363 on low back pain in DDD patients. In this communication, demographic, baseline and safety data are presented.

FIGURE 1. Schematic illustration of the transformation of the unstable disc with inflamed nucleus pulposus into a stabilised disc with fibrotic nucleus after injection of STA363



METHODS

With a power of 80% and p<0.10, 110 patients were required assuming a dropout rate of 10%. Average daily pain was reported on a numeric rating scale (NRS; 0-10) for 7 consecutive days. Prior to the start of the pain measurement, a placebo control reminder script was read to the patients. The script included for example information on the nature of the placebo response and urged the patients to report pain as truthfully as possible without speculating on what kind of treatment they had received. The purpose was to reduce the placebo response and a similar script has been used successfully in other studies on indications associated with a high placebo response[2]. Intradiscal injection of STA363 mixed with Omnipaque (1.5 mL/disc) was done under fluoroscopic guidance. Omnipaque was added to verify the accuracy of intradiscal injection and to detect possible leakage from the disc. Up to 2 lumbar discs of Pfirrmann grade 2 or 3 could be treated, and patients were randomly assigned to placebo or STA363 at 60 or 120 mg/mL. Primary completion time was 6 months and total follow-up time was 12 months.

RESULTS

Patient flow is shown in Fig. 2. The intended volume was successfully injected in all patients. Leakage of injected formulation from the disc was observed in 6 patients without any sequelae.

FIGURE 2. Patient flow

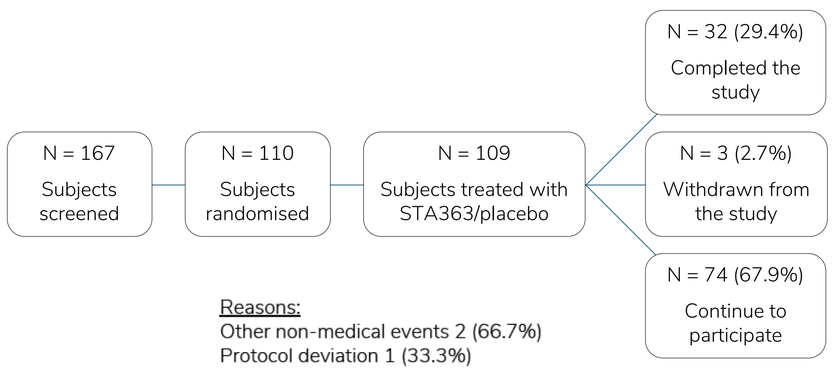


Table 1 shows the demographic data. The patient population was similar to that of other interventional studies in DDD patients, e.g., mean age was 41 years and there were slightly more women than men.

TABLE 1. Demographic characteristics of the included patients

Age (years)	Mean (Min – Max)	41.4 (21–67)
Gender	Male	51 (46.8%)
	Female	58 (53.2%)
Race/ethnic origin	Caucasian	108 (99.1%)
	African descent	1 (0.9%)
BMI (kg/m2)	Mean (Min – Max)	25.8 (16.3–43.4)

Treatment of L4/5 or L5/S1 accounted for 91% of the cases. One disc was treated in the majority of patients (63%) and all injected discs were of Pfirrmann grade 3 (Table 2).

TABLE 2. Baseline characteristics of the treated patients. Lowest and highest score represent the lowest and highest pain, respectively, reported by the patient during the 7-days pain measurement (NRS) period

		Number of patients (%)
Baseline pain intensity (NRS)	Lowest score 3-5	85 (78.0%)
	Lowest score 6-7	23 (21.1%)
	Lowest score 8-9	1 (0.9%)
	Highest score 3-5	26 (23.8%)
	Highest score 6-7	54 (49.5%)
	Highest score 8-9	29 (26.6%)
Number of treated discs	One	69 (63.3%)
	Two	40 (36.7%)
Treated disc level	L2/3	3 (2.0%)
	L3/L4	10 (6.8%)
	L4/L5	73 (49.3%)
	L5/S1	62 (41.9%)

Severe pain immediately after the injection was reported in about half of the cases, but pain abated rapidly (Table 3).

TABLE 3. Pain (NRS) after the intradiscal injection of STA363 or placebo

Pain assessment immediately after injection	Minimum	0
	Maximum	10
	Pain intensity ≥7	71/148 injections
Pain assessment 15 minutes after injection	Minimum	0
	Maximum	10
	Pain intensity ≥7	23/148 injections

There were 73 adverse events (AEs) in 48/109 (44%) treated patients (Table 4). Of these, 3 were serious but unlikely to be related to the study medication. Fifteen AEs were definitely related to the treatment and of these, 14 were post-injection pain. The majority (40/73) of AEs were mild, 30/73 were moderate and 3/73 severe (identical to the serious AEs).

TABLE 4. AEs by relatedness and intensity

	Not related	Unlikely related	Possibly related	Probably related	Definitely related	Total
Mild	12	8	13	4	3	40
Moderate	13	3	1	1	12	30
Severe	0	3	0	0	0	3
Total	25	14	14	5	15	73

CONCLUSION

With 109 treated patients, out of which 32 have completed the study and 40 have passed the 6 months but not 12 months follow-up, it can tentatively be concluded that intradiscal treatment with STA363 has a favourable safety and tolerability profile.

[1]Olmarker K, Gerward A, Isberg B, Lehmann A, Berg S (2020) Translational studies on biologic fusion of a vertebral segment as a novel treatment modality for low back pain. Spine 45, E1636-44.

[2]Cohen EA, Hassman HH, Ereshefsky L et al. (2021) Placebo response mitigation with a participant-focused psychoeducational procedure: a randomized, single-blind, all placebo study in major depressive and psychotic disorders. Neuropsychopharmacol. 46, 844–850.