A prospective, non-comparative clinical investigation for reconstruction of the ACL (24-month follow-up)

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Introduction

The OrthoPure® XT device is a porcine tendon graft which has been treated using a patented decellularisation processing technology (dCELL®) to remove all viable cells and native components which have the potential to elicit an immune response. This decellularisation technology gently cleanses the tissue whilst preserving the natural collagen architecture.

The OrthoPure® XT is an off-the-shelf device for knee ligament reconstruction that negates the need to take tissues from the patient, or to invest in complex and costly donor procurement processes. The result is a reduction in operative time, no donor site morbidity and associated muscle strength deficiencies for the patient, no specialist storage requirements and the flexibility to have the product ready to use off the shelf at any time.

The OrthoPure® XT device is a soft tissue graft that is specifically designed to be implanted using standard surgical techniques. It is compatible with standard instrumentation and with common soft tissue fixation devices for both femoral and tibial attachment. The handling properties are also comparable to commonly used soft tissue grafts (allograft or autograft).

Clinical study

Purpose

The purpose of this study was to assess the safety and performance of the OrthoPure® XT device when used for primary ACL reconstruction. This study was a prospective, non-comparative, single-arm, multicentre study.

Methods

40 subjects were treated for primary ACL reconstruction with the OrthoPure® XT device between November 2015 and August 2016 across 8 centres in Europe (age 18–48, mean 31.9 years, 28 males, 12 females, centres in UK, Poland and Spain).

Patients were included in the study if they met the following criteria: (1) 18 years old or older; (2) partial or complete tear of ACL requiring surgery; (3) passive flexion 120° and passive extension the same on both knees; (4) medial collateral ligament (MCL) injury grade 2 or less; (5) osteoarthritis grade 2 or less on the Kellgren Lawrence scale; and (6) ability to communicate meaningfully, willingness and ability to comply with study procedures.

All subjects were required to follow a rehabilitation programme following treatment, including a progressively increasing regime for a minimum of 4 and maximum of 6 months with the goal of returning the subject to their pre-injury levels of activity.

Endpoints were assessed at baseline screening and follow-up assessments at 3, 6, 12, and 24 months, as follows:

- Improvement of knee stability (primary endpoint) was assessed in comparison to the contralateral knee using an arthrometric ligament testing device (GNRB® system), and in comparison to the baseline (screening) assessment using the Lachman and Pivot Shift tests.
- Improvement in knee function (secondary endpoint) was assessed in comparison to the baseline (screening) assessment using International Knee Documentation Committee (IKDC) form, Lysholm score and Knee Injury and Osteoarthritis Outcome Score (KOOS).

- Safety was assessed by the rate of device-related adverse events (AE) and serious adverse events (SAE), the need for surgical reintervention and frequency of complications following surgery.

Statistical tests of significance were applied using a paired t-test or 2-sided Wilcoxon Signed Rank test, where a p-value of <0.05 was considered to be statistically significant. For arthrometric measurements, the anterior displacement (mm) between the operated and contralateral knee were tested for equivalence (± 3 mm margin). For analysis of missing data points, the last observation was carried forward. Sensitivity analysis did not show any changes to study outcomes for actual vs augmented data and therefore only actual data collected is presented.

Results

Device safety

The type, pattern, frequency and severity of safety events reported were considered typical following ACL reconstruction with allograft and autograft. 5 SAE were related to granuloma, synovitis and inflammation which were related to the use of a bioresorbable screw for fixation. All events were resolved by removal of the screw. 2 subjects were reported as having an ACL rupture (1 traumatic and 1 atraumatic), and an additional subject that has been lost to follow-up has since reported ACL reconstruction failure.

Device performance

Of the 40 subjects treated with the device, 34 remained at the 24-month follow-up. 6 subjects were terminated early: 2 lost to follow-up, 2 withdrew consent and 2 graft ruptures. 1 subject's data was also excluded from the assessment of device performance due to a major protocol deviation.

Of the data collected, the mean side-to-side difference (SSD) was 2.49 mm ± 1.46 mm. 19/29 subjects (65.5%) had an SSD of ≤ 3 mm. 1/29 (3.4%) had an SSD of > 5 mm. Statistical equivalence in SSD was shown ($p<0.001$).

Figure 1 shows the Lachman score distribution at baseline and 24-month follow-up assessment. A statistically significant improvement from baseline was reported ($p<0.001$).

Lachman score	Baseline	24 months
Negative (normal)	1	22
dnearly normal)	5	8
Positive ++ (abnormal)	27	3
Positive +++ (severely abnormal)	7	1
No data	0	6

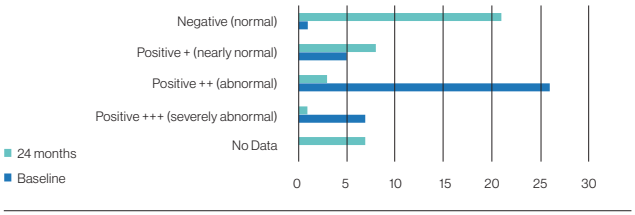

Figure 1. Lachman score results at 24-month follow-up.

Figure 2 shows the Pivot Shift Test distribution at baseline and 24-month follow-up assessment. A statistically significant improvement from baseline was reported (p<0.001).

Pivot Shift Test	Baseline	24 months
Negative	4	26
Positive	36	8
No data	0	6

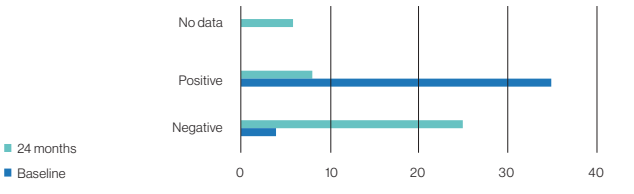

Figure 2. Pivot Shift Test results at 24-month follow-up.

Of the data collected, the average IKDC score was 91.0 ± 9.3, compared to 54.6 at baseline. A statistically significant improvement from baseline was reported (p<0.001).

Of the data collected, the average Lysholm score was 95.1 ± 7.4, compared to 66.3 at baseline. A statistically significant improvement from baseline was reported (p<0.001).

Figure 3 shows the KOOS score distribution at baseline and 24-month follow-up assessment. A statistically significant improvement from baseline was reported (p<0.001).

KOOS assessment	Baseline	24 months
Symptoms	78	97
Pain	74	98
Function in daily living	84	99
Function in sports recreation	44	93
Knee-related quality of life	34	82

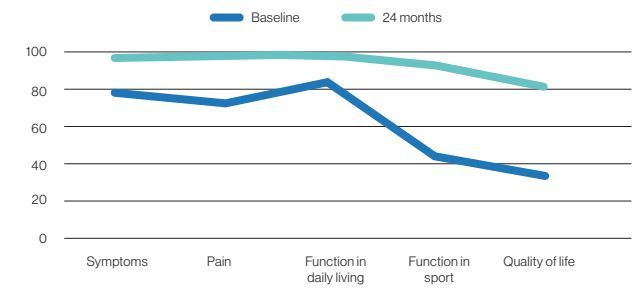

Figure 3. KOOS results at 24-month follow-up.

Ease of use of the device was assessed by the investigator at the point of use and is summarised in Figure 4.

Product attribute	Excellent	Good	Fair	Poor
Amount of material available	32	8	0	0
Ease of implantation	30	10	0	0
Ease of fixation	35	5	0	0
Overall product satisfaction	31	9	0	0

Figure 4. Ease of use assessment results.

Conclusions

Safety and performance data for the OrthoPure® XT device at the 24-month follow-up assessments has shown that the device is safe and performs as intended and is therefore a viable alternative to other tissue grafts.

Product information

Device size	Mean strength	Indication
5	900 N	• Multi-ligament reconstruction Recommended for use in: Extra-articular ligament reconstruction
6	1200 N	• Multi-ligament reconstruction Recommended for use in: Extra-articular ligament reconstruction
8	3500 N	• Primary anterior cruciate ligament (ACL) reconstruction where autograft tissue is not suitable • Revision ACL reconstruction • Multi-ligament reconstruction Recommended for use in: Extra-articular ligament reconstruction
10	5700 N	• Multi-ligament reconstruction Recommended for use in: Posterior cruciate ligament (PCL) reconstruction

Device size	Catalogue number
5	2405XTS
6	2406XTS
8	2408XTD
10	2410XTT

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