A phase I study of ICX-RHY, a suspension of allogeneic human dermal fibroblasts, administered intradermally

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Introduction

ICX-RHY is an injectable suspension of allogeneic human dermal fibroblasts being developed by Intercytex plc (Cambridge, UK) for use in facial rejuvenation. A phase I single-blind placebo-controlled study to assess safety, tolerability and histological change was conducted among ten adult volunteers.

Results

Subjects received ICX-RHY (3.2×10^7 human dermal fibroblasts in 800µL HypoThermosol®-FRS) and placebo (HypoThermosol®-FRS alone) concurrently by intradermal injection into the outer aspect of each upper arm. Injections were administered on three occasions at the same anatomic sites every 2-12 weeks.

Safety and tolerability were assessed throughout and a punch biopsy of the injection sites was taken for histological analysis two weeks following the final injection.

ICX-RHY was shown to be very well tolerated with no serious adverse events reported; no subject withdrew from the study. A total of 39 adverse events (AEs) were reported, of these, 28 were deemed "probably-related" to treatment. Twenty-two (79%) AEs were graded as mild in intensity with five (18%) moderate and one (4%) severe.

The five moderately intense AEs included induration, pain, oedema and inflammation and all five were seen among only two subjects. The only severe AE was a case of local inflammation following the second injection; this resolved spontaneously within one day. A summary of all treatment-related injection site AEs is shown in *Table 1*.

Table 1: Summary of injection site AEs

	AEs (n=28)	**Subjects** (n=10)
Induration	9 (32%)	7 (70%)
Pruritis	4 (14%)	3 (30%)
Erythema	3 (11%)	3 (30%)
Pain	3 (11%)	3 (30%)
Inflammation	3 (11%)	1 (10%)
Bruising	2 (7%)	2 (20%)
Oedema	2 (7%)	2 (20%)
Warmth	1 (4%)	1 (10%)
Discolouration	1 (4%)	1 (10%)

Sixteen (57%) of AEs were reported following the first injection with four (14%) and eight (29%) following the second and third injections respectively.

The timing of the onset of AEs was variable with all events becoming apparent within 12 days following injection except in one subject where local pain, redness and induration began 22 days post-injection. All AEs were self-limiting and resolved spontaneously with the exception of one mild episode of induration following the third injection which persisted to the final visit. All other events resolved within 23 days of onset. No treatment-related systemic AEs were reported and there were no significant clinical laboratory findings.

The skin biopsies showed a lymphocytic infiltrate confined to the subcutaneous fat with evidence of mild fat necrosis. Occasional histiocytes and plasma cells were seen and three biopsies showed significant numbers of eosinophils. Thickening of both the epidermis and dermis was observed with a marked increase in the number of dermal fibroblasts present (see *Fig 1* and *Fig 2* below).

Fig 1: Thickening of epidermis and dermis

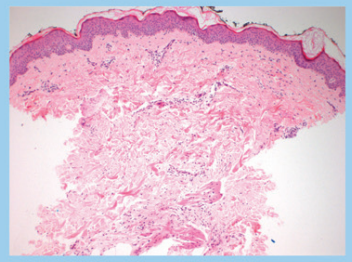
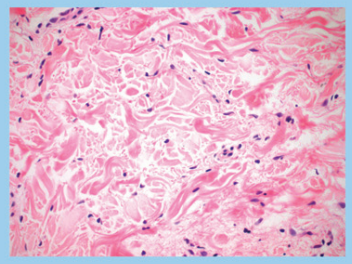


Fig 2: Increased dermal fibroblasts



Conclusion

This was the first study of ICX-RHY in man; it was very well tolerated with no unexpected or serious adverse events reported. There was evidence of both epidermal and dermal thickening with a marked increase in the number of dermal fibroblasts present. These findings support the further clinical development of ICX-RHY.

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