

Dupuytren's contracture* management: patient and physician perspectives

The 'Dupuytren's Summit' is a scientific meeting about Dupuytren's contracture, funded and organised by Pfizer and supported by FESSH (Federation of European Societies for Surgery of the Hand). The meeting was held for the second time on 15–16 March 2013 in Vienna, attended by approximately 250 hand surgeons. This year, 'Dupuytren's Summit 2013: Extending our reach together', covered a range of topics about the management of Dupuytren's contracture; one of these was around the patient and physician perspectives relating to the management of this condition.

Dupuytren's contracture – the patient perspective

Dr Maurizio Calcagni – Vice Chairman at the Division of Plastic Surgery and Hand Surgery and Head of the Hand Surgery and Research Unit, University Hospital Zurich, Switzerland; Lecturer in Plastic Surgery and Hand Surgery at the School of Medicine, University of Zurich, Switzerland.

Financial Disclosure: Dr Calcagni is a speaker and consultant for Pfizer. He was also an investigator for the Multicord study sponsored by Auxilium.

Wolfgang Wach – One of the chairmen of the International Dupuytren Society, a non-profit organisation where patients and clinicians collaborate (www.dupuytren-online.info).

Wolfgang Wach was unable to attend the summit and as such his presentation was delivered on his behalf by Prof Bert Reichert.

Financial Disclosure: This year's International Dupuytren Award, instituted by the International Dupuytren Society, is financially supported by Pfizer.

Whilst defining a typical patient is not straightforward, there are particular patient characteristics that are often associated with the disease such as being of white, northern European descent,¹ an older male (on average 55 years)^{1,2} and a smoker¹. Excessive alcohol intake^{3,4} and co-morbidities such as diabetes are also seen as risk factors for the disease.^{1,4}

Studies also suggest that important predictor factors exist in relation to disease severity and recurrence. These can include:^{5,6}

- » Early onset of disease (younger than 50 years)
- » A family history of the disease
- » Presence of ectopic lesions
- » Presence of knuckle pads
- » Bilateral hand involvement
- » Plantar fibrosis

The choice of treatment for Dupuytren's contracture involves many factors and should be determined in consultation with the patient, with many surgeons currently basing the decision on their own experience and intuition due to a lack of clinical guidelines. Each patient with Dupuytren's contracture is reviewed on a case by case basis and the type of treatment administered will be appropriate for that patient. It is crucial for patients to have access to the necessary information about treatments so they can have informed discussions with their doctor.

Each patient with Dupuytren's contracture has a different experience in terms of nature and severity of the disease and the goals of treatment will vary from patient to patient, for example, for some patients the goal will be full correction, for others partial correction that increases hand function will be sufficient, and for others relief of pain and discomfort may be the major aim. However, patient satisfaction is the ultimate goal, and managing patient expectations is an important part of this.

Dupuytren's contracture – the physician perspective

Mr David Warwick – Consultant Hand Surgeon at University Hospital Southampton and University of Southampton, UK since 1998. Recently published a comprehensive review of Dupuytren's disease and treatments.⁷

Financial Disclosure: Mr Warwick has advised Pfizer and received consultancy payment. He has received funding for participating in lectures and workshops. His attendance at the American Society for Surgery of the Hand meeting in 2011 was sponsored by Pfizer.

The shifting treatment paradigm: Why have I changed how I treat patients with Dupuytren's contracture? – Mr D. Warwick

Treatment options for Dupuytren's contracture have changed over the last few years, with recent non-surgical treatments giving surgeons the opportunity to reconsider the treatment paradigm.

Mr Warwick says, "For patients with an isolated palpable cord and good skin cover, I now tend to treat with collagenase clostridium histolyticum (CCH), and for those with dense disease or scarring, a skin graft."

Clinical studies have shown CCH to be an effective and well-tolerated treatment for Dupuytren's contracture with a palpable cord,^{8,9,10} and this has been seen in Mr Warwick's clinical practice.

Most commonly reported adverse events are injection site skin tears and blisters but patients generally recover within 1–2 weeks of injection.⁹ Cases of tendon rupture, tendonitis, ligament injury and complex regional pain syndrome were also reported, but uncommon.⁹

Recurrence may occur after CCH.¹¹ If so, Mr Warwick suggests that it can be treated with another injection. Further to this, he feels that surgery after previous CCH is not compromised (although no clinical data are available to support this at this stage).

Dermofasciectomy with full thickness skin grafting offers a low recurrence rate for treatment of Dupuytren's contracture.^{12,13,14} In Mr Warwick's opinion, if the surgery is undertaken carefully, it is as straightforward as simple fasciectomy and recovery is as quick. It is particularly suitable for patients with dense disease or scars who would not be suitable for CCH. Furthermore, Mr Warwick currently believes that because revision surgery is technically much more difficult with a higher chance of complication, the threshold for a primary skin graft at the first operation should be low and is often preferable to a primary fasciectomy.

The shifting treatment paradigm: Why haven't I changed how I treat patients with Dupuytren's contracture? – Prof J. Dias

Professor Joseph Dias – Professor in Hand and Orthopaedic Surgery and Head of Division of Orthopaedic Surgery at the University of Leicester, UK; Consultant Hand and Orthopaedic Surgeon for the University Hospitals of Leicester, UK.

Financial Disclosure: Professor Dias has advised Pfizer and received consultancy payment.

Professor Dias notes that many patients are aware of CCH as a treatment option through the popular press and the internet, and that they often believe both that the procedure is well tolerated and that outcomes are good and lasting.**

Professor Dias does not yet offer CCH as a treatment. He explains that appropriate education of patients will be key to the successful introduction of CCH into his practice. There are various reasons why he has not yet included CCH

**No published evidence available

XIAPEX®
Abbreviated Prescribing Information: (See Xiapex Summary of Product Characteristics for full Prescribing Information)

Presentation: Powder and solvent for solution for injection for intraligamentary use. The vial of powder contains 0.9mg collagenase clostridium histolyticum. The powder is a white lyophilised powder and the solvent is a clear colourless solution. **Indications:** Treatment of Dupuytren's contracture in adult patients with a palpable cord.

Dosage: Xiapex must be administered by a physician appropriately trained in the correct administration of the product and experienced in the diagnosis and management of Dupuytren's disease. The recommended dose of Xiapex is 0.58mg per injection into a palpable Dupuytren's cord. For an MP joint, each dose is administered in an injection volume of 0.25ml (requiring 0.39ml solvent for reconstitution). For a PIP joint, each dose is administered in an injection volume of 0.20ml (requiring 0.31ml solvent for reconstitution). Approximately 24 hours after injection, a finger extension procedure may be performed to facilitate cord disruption. If a satisfactory response has not been achieved, injections and finger extension procedures may be repeated up to 3 times per cord at approximately 4-week intervals. Only one cord must be treated at a time. **Contraindications:** Hypersensitivity to the active substance or to any of the excipients.

Warnings and Precautions: Allergic reactions – 17% of Xiapex-treated patients in phase 3 placebo-controlled clinical studies had mild allergic reactions (i.e. pruritus). Physicians must be prepared to address any severe local or systemic allergic reactions including the potential for anaphylaxis following injection, including the potential for such reactions following repeated use. Whilst there is no evidence from the clinical data of an increased risk of serious allergic reactions upon repeated injections, the potential for such reactions following repeated use cannot be excluded. Tendon rupture or other serious injury to the injected extremity – Injection of Xiapex into collagen containing structures of the hand other than the

Dupuytren's cord may result in damage to those structures including possible tendon rupture or ligament damage. Injections into cords affecting the PIP joint of the 5th finger must not be more than 2 to 3 mm in depth and nor more than 4mm distal to the palmar digital crease. Patients should be instructed to contact their physician in case of symptoms of tendon rupture. Use in patients with coagulation disorders – Xiapex must be used in caution in patients with coagulation disorders or those taking anticoagulants. Use of Xiapex in patients who have received anticoagulants (with the exception of up to 150mg acetylsalicylic acid daily) within 7 days prior to receiving an injection of Xiapex is not recommended. Immunogenicity – As with any non-human protein medicinal product, patients may develop antibodies to the therapeutic protein. Since the enzymes in Xiapex have some sequence homology with human matrix metalloproteinases (MMPs), anti-drug antibodies could theoretically interfere with human MMPs. No safety concerns related to the inhibition of endogenous MMPs have been observed, in particular no adverse events indicating the development or exacerbation of autoimmune diseases or the development of a musculoskeletal syndrome but the potential for it to occur cannot be excluded. If this syndrome were to develop, it would occur progressively and is characterized by one or more of the following signs and symptoms: arthralgia, myalgia, joint stiffness, stiffness of the shoulders, hand oedema, palmar fibrosis and thickening or nodules forming in the tendons. Long-term safety – Long-term safety of Xiapex is not fully characterised. The impact of treatment with Xiapex on subsequent surgery, if needed, is not known. **Drug Interactions:** Use of Xiapex in patients who have received tetracycline antibiotics e.g. doxycycline, within 14 days prior to receiving an injection of Xiapex is not recommended. **Pregnancy & Lactation:** Not recommended in pregnancy. Xiapex can be used during breast feeding. **Driving and operating machinery:** Xiapex may have a major influence on the ability to drive and use machines due to swelling and pain in the treated hand. Other minor influences include dizziness, paraesthesia,

hypoesthesia, and headache, see side effects. Patients must be instructed to avoid potentially hazardous tasks such as driving or using machines until it is safe to do so or as advised by the physician.

Side Effects: In clinical trials, the most frequently reported adverse reactions during the Xiapex were local injection site reactions such as oedema peripheral (local to the injection site), contusion (including ecchymosis), injection site haemorrhage and injection site pain. Injection site reactions were very common, occurring in the vast majority of patients, were mostly mild to moderate in severity and generally subsided within 1–2 weeks post injection. Serious adverse reactions of tendon rupture, tendonitis, other ligament injury and complex regional pain syndrome related to the medicinal product were reported. Very commonly reported adverse reactions include lymphadenopathy, pruritus, ecchymosis, pain in extremity, oedema peripheral (including injection site oedema and oedema), injection site haemorrhage, injection site pain, injection site swelling, tenderness, contusion. Commonly reported adverse reactions include lymph node pain, paraesthesia, hypoesthesia, burning sensation, dizziness, headache, nausea, blood blister, blister, rash, erythema, hyperhidrosis, arthralgia, joint swelling, myalgia, axillary pain, inflammation, injection site inflammation, swelling, injection site erythema, injection site pruritus, injection site warmth, injection site vesicles, skin laceration.

Overdose: Overdose is expected to be associated with increased local injection site reactions. Provide routine supportive care and treat symptomatically.

Legal Category: POM. **Marketing authorisation holder:** Pfizer Ltd, Ramsgate Road, Sandwich, Kent, CT13 9NJ, UK. **Package quantities, Marketing Authorisation numbers and basic NHS price:** XIAPEX 0.9mg powder and solvent for solution for injection, EU/1/11/671/001, £650.00. **Further information is available on request from:** Medical Information at Pfizer Limited, Walton Oaks, Dorking Road, Tadworth, Surrey, KT20 7NS, UK. Tel: +44 (0) 1304 616161 Date of Preparation: October 2012. Company reference: XP2_0

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to your local Pfizer office.

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