

New Pulmonary Fibrosis Treatments in Pipeline

BY MARY ELLEN SCHNEIDER
Senior Writer

NEW YORK — Physicians may be getting more options for the treatment of idiopathic pulmonary fibrosis as more therapies come down the research pipeline, Dr. Paul F. Simonelli said at a conference on pulmonary and critical care medicine sponsored by Columbia University.

Among the therapies under evaluation in recently completed or ongoing clinical

trials for idiopathic pulmonary fibrosis (IPF), are interferon-gamma-1b, N-acetylcysteine, bosentan, etanercept, and imatinib. In addition, there are some molecules, such as pirfenidone, being tested that currently have no other approved uses, said Dr. Simonelli of Columbia University (New York).

The development of new therapies is critical because there are no approved treatments for IPF and the standard approaches are not getting results, he said.

“IPF is a serious disease. It’s a debilitating disease, and up to now we’ve had no effective therapy,” Dr. Simonelli said.

The prevalence of the disease is about 83,000 cases in the United States with about 31,000 new cases each year. And the disease has a mortality worse than that of almost any other major disease, except lung cancer. Patients with IPF face a 5-year survivorship of less than 50%, Dr. Simonelli said.

The majority of available data relates to

the use of interferon-gamma-1b in IPF. An earlier phase III trial of about 330 patients showed no difference between the drug and placebo for the trial’s primary endpoint of progression-free survival (N. Engl. J. Med. 2004;350:125-33). However, a subgroup analysis indicated possible survival benefits with the drug. A second phase III trial looking at survival as the primary endpoint is underway, and the drug maker InterMune is recruiting patients.

A European study showed promising results for N-acetylcysteine in treating IPF. The drug showed improvement in vital capacity and diffusing capacity compared to treatment with prednisone and azathioprine (N. Engl. J. Med. 2005;353:2229-42). But Dr. Simonelli said the results are hard to interpret since the standard of care in Europe is the use of prednisone and azathioprine instead of a true placebo.

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Another much-discussed possible treatment is pirfenidone. Three trials have been conducted on the drug—an open-label phase II trial in North America, a Japanese trial stopped early because patients on placebo were experiencing severe exacerbations, and a third trial ongoing in Europe. Additional trials of the drug are expected to begin in the United States sometime this year. ■



BRIEF SUMMARY

Please consult package insert for full Prescribing Information.

INDICATION

EUFLEXXA™ (1% sodium hyaluronate) is indicated for the treatment of pain in osteoarthritis (OA) of the knee in patients who have failed to respond adequately to conservative non-pharmacologic therapy and simple analgesics (e.g., acetaminophen).

CONTRAINDICATIONS

- Do not use EUFLEXXA™ to treat patients who have a known hypersensitivity to hyaluronan preparations
- Do not use EUFLEXXA™ to treat patients with knee joint infections, infections or skin disease in the area of the injection site

WARNINGS

- Mixing of quaternary ammonium salts such as benzalkonium chloride with hyaluronan solutions results in formation of a precipitate. EUFLEXXA™ should not be administered through a needle previously used with medical solutions containing benzalkonium chloride. Do not use disinfectants for skin preparation that contain quaternary ammonium salts
- Do not inject intravascularly because intravascular injection may cause systemic adverse events

PRECAUTIONS

General

- Patients having repeated exposure to EUFLEXXA™ have the potential for an immune response; however, this has not been assessed in humans
- Safety and effectiveness of injection in conjunction with other intra-articular injectables, or into joints other than the knee has not been studied
- Remove any joint effusion before injecting
- Transient pain or swelling of the injected joint may occur after intra-articular injection with EUFLEXXA™
- Do not use after expiration date
- Protect from light
- Do not re-use—dispose of the syringe after use
- Do not use if the blister package is opened or damaged

Information for Patients

- Transient pain and/or swelling of the injected joint may occur after intra-articular injection of EUFLEXXA™
- As with any invasive joint procedure, it is recommended that the patient avoid any strenuous activities or prolonged (i.e., more than 1 hour) weight-bearing activities such as jogging or tennis within 48 hours following intra-articular injection
- The safety and effectiveness of repeated treatment cycles of EUFLEXXA™ have not been established

ADVERSE EVENTS

Adverse event information regarding the use of EUFLEXXA™ as a treatment for pain in OA of the knee was available from two sources; a multicenter clinical trial conducted in Germany and a single center clinical trial that was conducted in Israel.

Multicenter Clinical Investigation

This clinical investigation was a prospective randomized, double blinded, active control (commercially available hyaluronan product) study conducted at 10 centers. Three hundred twenty-one patients were randomized into groups of equal size to receive either EUFLEXXA™ (n=160) or the active control (n=161). A total of 119 patients reported 196 adverse events; this number represents 54 (33.8%) of the EUFLEXXA™ group and 65 (44.4%) of the active control group. There were no deaths reported during the study.

Incidences of each event were similar for both groups, except for knee joint effusion, which was reported by 9 patients in the active control group and one patient in the EUFLEXXA™ treatment group. A total of 160 patients received 478 injections of EUFLEXXA™. There were 27 reported adverse

events considered to be related to EUFLEXXA™ injections: arthralgia – 11 (6.9%); back pain – 1 (0.63%); blood pressure increase – 3 (1.88%); joint effusion – 1 (0.63%); joint swelling – 3 (1.88%); nausea – 1 (0.63%); paresthesia – 2 (1.25%); feeling of sickness of injection – 3 (1.88%); skin irritation – 1 (0.63%); tenderness in study knee – 1 (0.63%). Four adverse events were reported for the EUFLEXXA™ group that the relationship to treatment was considered to be unknown: fatigue – 3 (1.88%); nausea – 1 (0.63%).

Single Center Study

In a single-center, single-blinded, placebo controlled, prospective, two parallel treatment arm clinical trial a total of 49 (25 EUFLEXXA™, 24 placebo) patients were randomized into two treatment groups in a ratio of 1:1 EUFLEXXA™ or placebo. A total of 65 adverse events were reported by 17 (68%) of the patients in the EUFLEXXA™ group and 15 (63%) in the placebo group. Of the 65 total events reported, 20 were regarded as treatment related. Knee pain, hypokinesia of the knee, knee swelling, and rash were considered to be treatment related adverse events.

DETAILED DEVICE DESCRIPTION

Each syringe of EUFLEXXA™ contains:

Sodium hyaluronate	20 mg
Sodium chloride	17 mg
Disodium hydrogen phosphate dodecahydrate	1.12 mg
Sodium dihydrogen phosphate dihydrate	0.1 mg
Water for injection	q.s.

HOW SUPPLIED

EUFLEXXA™ is supplied in 2.25 ml nominal volume, disposable, pre-filled glass syringes containing 2 ml of EUFLEXXA™. Only the contents of the syringe are sterile. EUFLEXXA™ is nonpyrogenic.

CAUTION

Product contact parts of the syringe contain natural rubber latex, which may cause allergic reactions.

DIRECTIONS FOR USE

- Store refrigerated at 2°-8°C (36°-46°F). Protect from light.
- EUFLEXXA™ is administered by intra-articular injection into the knee synovial capsule using strict aseptic injection procedures. The full content of the syringe is injected into the affected knee at weekly intervals for 3 weeks, for a total of 3 injections.
- Twenty to thirty minutes before use, remove the product box from the refrigerator, remove the blister pack from the box and allow the syringe to come to room temperature. Be sure to return any syringes not intended for use to the refrigerator.

Toll free number for providers and patients to call with questions: 1-(888)-FERRING (1-(888)-337-7464).

MANUFACTURED FOR:

FERRING
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Reference: 1. Kirchner M, Marshall D. A double-blind, randomized, controlled trial comparing alternate forms of high molecular weight hyaluronan for the treatment of osteoarthritis of the knee. *Osteoarthritis Cartilage*. In press.

Variants Key

Metabolic Link from page 1

High numbers of lesions also correlated with increases in erythrocyte sedimentation rate and C-reactive protein levels.

A total of 78% patients had the plaque variant of morphea, with the remainder having the guttate variant, idiopathic atrophoderma of Pasini and Pierini, linear scleroderma, and profound scleroderma.

In patients with all variants of morphea, lesions were found on the trunk in 81%, while facial lesions were seen in only eight patients. Overlap syndromes also were reported; eight patients had morphea and lichen sclerosus et atrophicus, and two had morphea with eosinophilic fasciitis.

“Our data also suggest the existence of variant-specific organ involvement in morphea,” Dr. Pfeiffer said. Arthralgias were reported by 40% of patients with atrophoderma Pasini and Pierini, while linear scleroderma was associated with the presence of antinuclear antibodies, muscular atrophy, and contractures. Among patients with profound scleroderma, 45% had myalgias and myopathy.

There were no increases in Raynaud symptoms, carpal tunnel syndrome, or lung disorders in patients with any of the variants, she said. ■