3 Minute KINERET Product Testimonial

My name is ___ , a (title) and employee of Sobi, Inc. the North American affiliate of Sobi AB, an international biopharmaceutical company dedicated to rare disease. This testimonial will be used for presentation purposes and will not be distributed or copied without prior approval from Sobi Inc.

I am here today to discuss the biologic drug KINERET® (anakinra), an FDA approved interleukin-1 receptor antagonist. Anakinra is a recombinant, non-glycosylated form of the human interleukin-1 receptor antagonist (IL-1Ra) with an additional single methionine residue on the amino terminus[1]. Like the endogenous IL-1Ra protein, anakinra is a competitive inhibitor of the proinflammatory cytokine IL-1[2,3]. Anakinra has a 4-6 hour half-life and ability to penetrate the central nervous system, two pharmacokinetic properties that make anakinra beneficial. Anakinra is supplied in 100 mg single use syringes for subcutaneous self-administration[1].

Anakinra is FDA approved for three indications: rheumatoid arthritis (RA), Neonatal-Onset Multisystem Inflammatory Disease (NOMID) and Deficiency of Interleukin-1 Receptor Antagonist (DIRA)[1].

Specifically, anakinra is approved to reduce the signs and symptoms and slow the progression of structural damage in moderately to severely active rheumatoid arthritis, in patients 18 years of age or older who have failed 1 or more disease modifying antirheumatic drugs[1]. Rheumatoid arthritis is the most common type of autoimmune arthritis, characterized by chronic inflammation of synovial tissue, which can lead to joint destruction. The primary goal of treatment is to control pain and inflammation, reduce joint damage and disability.[4]

The safety and efficacy of KINERET was evaluated in three randomized, double-blind, placebo-controlled trials of 1790 patients aged 18 years or greater with active rheumatoid arthritis[1]. Trial outcomes demonstrated improvements in ACR component scores, joint space narrowing (JSN) and erosion scores (ES) [1]. The recommended dose of anakinra for the treatment of patients with rheumatoid arthritis is 100mg/daily by subcutaneous injection[1].

Anakinra is the only FDA approved treatment for Neonatal-Onset Multi-inflammatory Disease (NOMID), a form of Cryopyrin-Associated Periodic Syndromes. NOMID is a rare, life-threatening disease causing persistent inflammation throughout the body from birth, or starting soon afterward[5]. Safety and efficacy was assessed in a clinical study of 43 NOMID patients, ages 0.7 to 46 years, treated for up to 60 months. Improvements occurred in all individual disease symptoms as well as in the serum markers of inflammation[1]. The recommended starting dose of anakinra is 1-2 mg/kg daily up to a maximum of 8 mg/kg daily to control active inflammation[1].

Anakinra is also approved for the treatment of Defiency of Interleukin-1 Receptor Antagonist (DIRA), which is an ultra-rare, autoinflammatory disease caused by a genetic mutation in the IL1RN gene, which encodes the interleukin-1 receptor antagonist (IL-1Ra) protein.[6] In patients with DIRA, the deficiency of IL-1Ra leads to unopposed action of IL-1 signaling, resulting in life-threatening systemic inflammation with skin and bone involvement.[6] Safety and efficacy were evaluated in a long-term natural history

study, including nine patients with DIRA (ages 1 month to 9 years at start of treatment) treated for up to 10 years. All nine patients achieved inflammatory remission while on treatment.[1] The recommended starting dose of anakinra is 1-2 mg/kg daily up to a maximum of 8 mg/kg daily to control active inflammation[1].

In summary, anakinra is indicated for the treatment of RA in patients 18 years of age or older who have failed 1 or more disease modifying antirheumatic drugs, NOMID and DIRA. The most common side effects of KINERET include injection site skin reactions, including redness, swelling, bruising, itching, and stinging. Common adverse reactions (incidence ≥ 5%) observed in RA patients include: injection site reaction, worsening of rheumatoid arthritis, upper respiratory tract infection, headache, nausea, diarrhea, sinusitis, arthralgia, flu like-symptoms, and abdominal pain[1].

- KINERET is contraindicated in patients with known hypersensitivity to *E. coli*-derived proteins, KINERET, or any components of the product.
-In RA, discontinue use if serious infection develops. In KINERET-treated NOMID patients, the risk of a NOMID flare when discontinuing KINERET treatment should be weighed against the potential risk of continued treatment. Do not initiate Kineret in patients with active infections.
-Use in combination with Tumor Necrosis Factor (TNF) blocking agents is not recommended.
-Hypersensitivity reactions, including anaphylactic reactions and angioedema, have been reported.
-Patients with DIRA may have an increased risk of allergic reactions, particularly in the first several weeks after starting treatment.
-The impact of treatment with KINERET on active and/or chronic infections and the development of malignancies is not known.
-Live vaccines should not be given concurrently with KINERET.
-Neutrophil counts should be assessed prior to initiating KINERET treatment , and while receiving KINERET, monthly for 3 months, and thereafter quarterly for a period up to 1 year [1].

Please review full prescribing information before prescribing KINERET.

References-

1. KINERET® (anakinra) [package insert]. Stockholm, Sweden: Swedish (Sweden)Orphan Biovitrum (SOBI) Inc; 2020.
2. Benny Klimek M , et al. Effect of the IL-1 Receptor Antagonist Kineret on Disease Phenotype in mdx Mice. PLOS One 2016; 11(5): e0155944.
3. Dinarello C , et al. Treating inflammation by blocking interleukin-1 in a broad spectrum of diseases. Nat Rev Drug Discov. 2012; 11(8): 633–65
4. Ferro F, Elefante E, et al. One year in review 2017: novelties in the treatment of rheumatoid arthritis. Clin Exp Rheumatol 2017; 35(5):721-734.
5. Goldbach-Mansky R, Dailey NJ, et al. Neonatal-onset multisystem inflammatory disease responsive to interleukin-1 beta inhibition. N Engl J Med 2006; 355(6):581-92.
6. Aksentijevich I, et al. An Autoimmune Disease with Deficiency of the Interlueikin-1 -Receptor Antagonist. N Engl J Med 2009; 360(23):2426-3