

The Recent Sarilumab Phase III Clinical Result:

What Do You See in These Three Articles Written About the Same Story?

Spend ~10 minutes reading the next three slides and circle everything you consider to be noteworthy. We will spend the first part of class Monday discussing. Be ready to be called on!

Sarilumab Phase 3 Report (1 of 3)

Sanofi has experienced a series of internal setbacks on the R&D front in recent months, but its close partnership with Regeneron is still paying off with promising late-stage data. Friday morning, the companies reported that two doses of the anti-IL-6R blocker sarilumab easily beat out a placebo in the first of a string of Phase III studies for rheumatoid arthritis. The two doses in the study improved patient ratings on the signs and symptoms of the disease after 24 weeks of treatment for 66% of the patients in the 200 mg arm and 58% in the 150 mg dose arm, compared with 33% in the placebo arm. And the drug also passed co-primary endpoints for an improvement in physical function and inhibition in structural bone damage after a year of therapy. Sarilumab (REGN88/SAR153191) is billed as the first IL-6 drug in studies. Regeneron--which has been reaping a fortune from Eylea--used its own in-house tech to develop the antibody, which blocks IL-6 from binding to its receptor, interrupting a cascade of events that trigger rheumatoid arthritis. Two years ago, Regeneron green-lighted the late-stage program from RA but reported that a Phase II study for ankylosing spondylitis had failed. The partnership on sarilumab is one of a string of pacts that closely bind the pharma giant to the Tarrytown, NY-based biotech, which has enjoyed a R&D record in recent years. The collaboration includes dupilumab (REGN668), an IL-4 receptor treatment for allergic asthma and atopic dermatitis, as well as the blockbuster PCSK9 tie-up for alirocumab, which delivered the first positive results weeks ago. Those advances have helped take some of the sting out of Sanofi's setbacks on the cancer front, with back-to-back failures for its top two oncology programs in recent months. Regeneron and Sanofi developed the cancer drug Zaltrap but found only weak demand for the therapy, which had to be discounted after the price triggered a backlash among some prominent oncologists. "Irreversible joint damage can be a consequence for patients suffering from rheumatoid arthritis, and this is accompanied by reduced physical function in these patients," said Tanya Momtahn, sarilumab global project head at Sanofi. "This remains a major concern for rheumatoid arthritis patients. We are encouraged by these Phase III results and the impact sarilumab demonstrated on inhibition of progression of structural damage assessed radiographically in this study."

Sarilumab Phase 3 Report (2 of 3)

(Reuters) - An experimental drug for rheumatoid arthritis developed by French drugmaker Sanofi and Regeneron, when combined with methotrexate, improved symptoms and physical function and slowed progression of the disease in a late-stage clinical trial. Rheumatoid arthritis is an autoimmune disease in which the body's immune system mistakenly attacks healthy tissue, causing inflammation and pain in the joints. Sanofi and Regeneron's drug, called sarilumab, is an injectable antibody that works by blocking an inflammation-causing protein called interleukin 6. It is similar to Actemra, Roche's fast-growing treatment approved in 2010. The success of the trial pushes the new drug one step closer to the production line, although it still to pass further long-term trials and the approval process in particular markets. The 52 week SARIL-RA-MOBILITY Phase 3 trial enrolled some 1,200 patients with active, moderate-to-severe rheumatoid arthritis, who have not benefited from or been able to tolerate the standard oral treatment, methotrexate, whose side effects can include nausea and liver damage. Patients given a 200 mg dose of sarilumab every other week on top of methotrexate saw a 66 percent improvement in signs and symptoms of rheumatoid arthritis after six months, Sanofi and Regeneron said in a statement on Friday. Those given a 150 mg dose saw a 58 percent improvement, while those given a placebo alongside methotrexate saw a 33 percent improvement. Sarilumab met the other two primary endpoints of the study, improving physical function at week 16 and inhibiting progression of joint damage after one year, the companies said. Infections were the most frequently reported adverse side effects, as well as increases in "bad" LDL cholesterol and transaminases, they added. Sarilumab, alongside cholesterol drug alirocumab, is one of the promising products Sanofi is developing under its partnership with U.S. biotech Regeneron to offset the loss of patents on once top-selling drugs like blood thinner Plavix.

Sarilumab Phase 3 Report (3 of 3)

Sanofi and Regeneron's experimental rheumatoid arthritis drug eased symptoms and damage caused by the disease in a clinical trial, advancing its prospects in a market of new anti-inflammatory therapies led by Roche. In a study of 1,200 patients for whom the standard treatment methotrexate (MTX) was not sufficient, sarilumab plus MTX eased pain and stiffness twice as much as those who got MTX alone, and slowed joint destruction 90 percent more, the two companies said in a joint statement today. The trial is one of two that Paris-based Sanofi plans to use to seek regulatory approval for sarilumab. The drug may generate sales of \$780 million by 2020, according to the average of four analyst estimates compiled by Bloomberg. It would compete with Roche's Actemra and other experimental treatments in development by AbbVie, J&J and BMS. The study evaluated three groups of patients who received, in combination with MTX, either a 200 milligram or 150 milligram dose of sarilumab, or placebo. Among those in the study receiving the highest dose of sarilumab, 14 percent withdrew from the trial because of side effects, compared with 5 percent of those on MTX alone. Infections were also more common among those on Sanofi's drug. RA causes inflammation of the joints, often in the hands and feet. It is thought to be caused by problems with the immune system, according to the CDC. About 1.5 million people in the U.S. have it, according to the Arthritis Foundation. Patients typically start treatment with MTX, a cheaply available generic drug. If MTX doesn't work or becomes less effective, doctors can add a therapy such as AbbVie's best-selling drug Humira or Pfizer Inc.'s Enbrel. There's no cure for the chronic disease. Sanofi gained sarilumab as part of an alliance with the Tarrytown, New York-based biotechnology company Regeneron, in which it owns a 17 percent stake. The drug targets a messenger protein called interleukin-6, or IL-6, that is over-produced by people with RA, contributing to joint damage and inflammation. Basel, Switzerland-based Roche's Actemra generated \$898 million in sales last year. AbbVie is developing a drug that targets IL-6, called ALX-0061, which it licensed from Ghent, Belgium-based Ablynx NV in September in a deal worth as much as \$840 million. Johnson & Johnson's drug is called sirukumab and Bristol-Myers' is called clazakizumab.

MIT OpenCourseWare
<http://ocw.mit.edu>

20.201 Mechanisms of Drug Actions
Fall 2013

For information about citing these materials or our Terms of Use, visit: <http://ocw.mit.edu/terms>.