IN brief

Europe's first copy-cat antibody

The first biosimilar versions of a monoclonal antibody have received a positive opinion from the European Medicines Agency (EMA), paving the way for cheaper versions of expensive biologic drugs to enter the market. On June 28, the EMA's Committee for Medicinal Products for Human Use (CHMP) recommended Inflectra and Remsima, both containing infliximab, similar to the biological therapy best-seller Remicade, made by Merck of Whitehouse Station, New Jersey, and marketing partner J&J of New Brunswick, New Jersey. Infliximab is a chimeric human-murine IgG that neutralizes tumor necrosis factor alpha, an inflammation-promoting protein. The antibody copies are produced by Celltrion of Incheon City, South Korea, and Hospira, of Lake Forest, Illinois. The CHMP recommended Inflectra and Remsima for the same indications as Remicade: rheumatoid arthritis, Crohn's disease and psoriasis. Once the patent for Remicade expires in the EU next August, biosimilar sales are expected to make a severe dent in the $2 billion in revenues from sales of Remicade in Europe. In three to four years, Remicade biosimilars could capture about 40% of the EU market at about a 40% price reduction, says Bernstein analyst Ronny Gal in New York. Twelve biosimilars have been authorized in the EU since 2006, but Inflectra is the first structurally complex biologic. "We are not expecting that their approval will open 'floodgates,' but rather that the steady stream of applications for biosimilars will continue," says Martin Harvey Allchurch, EMA's head of communications. Celltrion has eight different monoclonal antibodies currently in development. *Emma Dorey*

IN their words

"Most of the time, couples don't find out that they carry these mutations until after the mother is already pregnant, or until after the child is born." Katrina Goddard, from Kaiser's Center for Health Research, the principal investigator on a $8.1-million, NIH-supported clinical trial that will sequence couples' complete genome before conception. (*Portland Business Journal*, 24 July 2013)

"NICE [National Institute for Health and Care Excellence] is not geared up for anything other than a pill every day for life, and that's where the system breaks down." Chris Mason, professor of regenerative medicine at UCL, commenting on a report that says the UK's system for evaluating drugs is not appropriate for cell-based therapies. (*The Guardian*, 30 June 2013)

Amgen best-seller challenged by generics

A recent clinical study found a combination of inexpensive drugs was as good as the biologic Enbrel (etanercept), from Amgen in Thousand Oaks, California, in treating patients with rheumatoid arthritis. Although small, this study comparing generic and branded drugs is an example of the upswing in comparative effectiveness research (CER), which could put pressure on many expensive drugs including biologics.

Generic drugs may be just as effective as branded biologics for treating rheumatoid arthritis.

The clinical trial was conducted by investigators affiliated with the US Department of Veterans Affairs and reported in *The New England Journal of Medicine* this summer (*NEJM* **369,** 307–318, 2013). The study enrolled 363 people, 90% of whom were white, who had active disease despite treatment with methotrexate, a common situation for this indication. Participants received a cocktail of three anti-rheumatic drugs—methotrexate combined with sulfasalazine and hydrochloroquine—or methotrexate with Enbrel. "The evidence here is not so strong," says Richard Gliklich of Quintiles Outcome, a research firm in Cambridge, Massachusetts, owing to the small study size and corresponding inability to look at subgroups that may perform better or worse than the average and the lack of patient heterogeneity. However, other studies of Enbrel "have moved in a similar direction even though their designs were different," he says. Eventually, that sum of information will make its way through professional society reviews, and perhaps also be picked up by internal technology assessment and review programs at payers. "If that happens, we'll see big changes," he says. "There is a risk here. I think this is a brush fire and you pay attention to brush fires because they might become a bigger fire."

As such, Amgen should be thinking about developing its own comparative effectiveness data, he says. "Others will do more studies because the differential in cost is so great and you don't want to be caught flat footed," Gliklich adds. Depending on additional data, payers may consider not allowing Enbrel until after the triple therapy tested in the *NEJM* study has been prescribed, for instance. "The onus will be on the manufacturers to demonstrate more and more effectiveness against other therapies," he says.

Some health plans are starting to use CER, says Rhonda Greenapple of Reimbursement Intelligence in Madison, New Jersey. But the pace has been slow. "Payers have the ability to do it," she says. Their fear is that physicians, patients or employers may ask why a patient is being denied a drug.

But the stage is set for CER to come of age. "When comparative effectiveness studies are well done and they are done in populations relevant to the majority of practice, and a difference is found, then I think they have a huge effect on practice," says Robert Califf of Duke University in Durham, North Carolina. Even when treatments are found to be comparable, as was the case in the Enbrel study, there could eventually be an impact on practice.

Biosimilars may have a more dramatic effect on treatment choices—potentially rendering the studies with nonbiologic agents (such as many of those comparing such agents to Enbrel) "irrelevant," note the authors of a commentary accompanying the Enbrel study in *NEJM*. Biosimilars "can more easily demonstrate that they are effective and cost effective to the practitioner to drive behavior," says Gliklich.

"The big gorilla" in pushing for more CER in the US, Califf says, is PCORI, the public-private patient-centered outcomes research initiative established through the Affordable Care Act of 2010 (*Nat. Biotechnol.* **30**, 482, 2012). PCORI has spent most of its time looking at different methodologies for doing CER, and has only limited resources to run big trials to get definitive answers about the comparative effectiveness of drugs. The National Institutes of Health is more likely to conduct the bigger CER studies needed to draw definitive conclusions.

Mark Ratner *Cambridge, Massachusetts*