

Mac-studied blood thinner getting closer to approval

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McMaster is closer to its "dream" of replacing the blood thinner warfarin with a drug that is more convenient for patients.

The university's second major study in four months is being published in the New England Journal of Medicine Thursday showing dabigatran is a safe and effective alternative to the commonly used blood thinner also known as Coumadin.

"Warfarin has been around for 60 years and it has been a dream to find something else," said Dr. Sam Schulman, McMaster professor and lead author of the study. "Dabigatran is a good alternative. That can change totally the picture in a few years of how patients are treated."

Called RE-COVER, the study shows dabigatran works as well as warfarin to treat potentially dangerous blood clots in the legs and lungs. It proved to be as safe , if not safer.

It was also used successfully to treat quivering hearts or atrial fibrillation in a McMaster study called RE-LY published in August.

The latest results were presented at the Annual Meeting of the American Society of Hematology yesterday and released early online by the journal.

Dr. Brian Gage, medical director of the Barnes-Jewish Hospital's Blood Thinner Clinic and an associate professor of medicine at Washington University in St. Louis calls the studies "quite significant."

"Warfarin is taken by two million North Americans each year. Up to now we've not had an oral alternative. It looks like dabigatran will be the first oral alternative."

Warfarin is a safe and effective blood thinner but it's inconvenient for patients. The drug requires constant monitoring so patients have to get blood tests anywhere from twice a week to once a month. Their doses change regularly.

Dabigatran also known as Pradax or Pradaxa requires no monitoring and the dose remains constant.

"That would be nice," said Allan Embey who was put on warfarin after heart surgery more than 10 years ago. "I wouldn't have to go for blood all the time."

The 51-year-old Port Dover man gets blood tests once to twice a month.

"I'm getting to know the people there too well," he jokes.

He would like to try dabigatran, but can't because the drug is heavily restricted in Ontario. It's currently only available for one month following hip or knee replacement surgery.

There is question about whether it will ever be in wide use because it costs about 14 times more than warfarin, which is less than \$1 a day.

"Warfarin is dirt cheap," said Schulman. However, he points out that doesn't take into account the price of monitoring patients.

"On the one hand, the drug is more costly and on the other hand, it's more convenient " agrees Gage.

The McMaster studies were paid for by drug company Boehringer-Ingelheim, which makes dabigatran.

RE-COVER compared six months of treatment with dabigatran to warfarin in 2,539 patients in 228 clinical centres in 29 countries.

While RE-LY showed that dabigatran could prevent blood clots, RE-COVER demonstrated that it could treat them. Venous thromboembolism affects one to two adults per 1,000 annually and is the third most common cause of vascular death.

"You have to treat it with something effective or the results can be disastrous," said Schulman." This shows it can be effective in the worst possible situation."

The randomized, double-blind study was difficult to do because researchers couldn't know which drug patients were taking but needed to closely monitor those on warfarin.

To do this, each patient took one of the drugs and a placebo of the other without knowing which was which.

Doctors gave all the patients the same blood tests they would give those on warfarin. The results were put into a computer that provided real results for those on warfarin and sham results for those on dabigatran. The doctors would adjust the warfarin doses without knowing if it was the real thing or the placebo.

The study found that both drugs were equally effective with just over 2 per cent of patients having recurrent venous thromboembolism. Rates of bleeding were similar or lower for dabigatran.

The drug's only side effect was heart burn and indigestion in a small number of patients.

This is the second drug Schulman has tested to replace warfarin. The first drug he studied was withdrawn in 2005 because of its effects on the liver.

This time Schulman and RE-LY principal investigator Dr. Stuart Connolly have a drug with a lot of promise.

"That's pretty exciting," said Gage.

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