Cystic Fibrosis Research News

Title:

Feasibility of placebo-controlled trial designs for new CFTR modulator evaluation

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What was your research question?

We wanted to know how willing patients that had access to the CFTR modulators Kalydeco® and Orkambi® and their doctors would be to participate in placebo-controlled clinical trials of new modulators that might someday replace these drugs. We wanted to know how the length of trials might influence willingness to participate.

Why is this important?

Several groups are developing newer CFTR modulator treatments that may have advantages over currently available modulators. More CFTR modulators should improve patient access and responses. Regulators approving new drugs often insist on clinical trial designs where patients are randomly assigned the new treatment or a placebo (sugar-pill). Patients participating in such trials will be required to stop taking Kalydeco® or Orkambi® and may end up receiving only placebo; they will no longer receive the benefits of these treatments. Willingness of patients currently treated with modulators to enrol in placebo-controlled trials will affect the design and feasibility of these trials.

What did you do?

We surveyed US CF doctors and their patients/family members currently receiving Kalydeco® or eligible to receive Orkambi® about their willingness to participate in placebo-controlled trials of a new CFTR modulator that would require them to stop taking any CFTR modulators during the trials. We asked whether they would be willing to enrol in studies of 2, 4, and 8 weeks, and also of 6 months if a) the new treatment was expected to have about the same effect as Kalydeco® or Orkambi® and b) if the new treatment was expected to have a better effect than the Kalydeco® or Orkambi®.

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What did you find?

For both patients/families with CF and their doctors, willingness to participate in placebo-controlled trials of new CFTR modulators was greatest for short (2 and 4 week) studies, and less for longer studies. Patients/families were more willing to participate in trials in which a new CFTR modulator was thought to be better than their current modulator and less willing if the new treatment was thought to be about the same as their current treatment. Patients taking Orkambi® were less willing to consider enrolling in placebo-controlled trials of new modulator treatments than those without current Orkambi® access.

What does this mean and reasons for caution?

Placebo-controlled trials will be important for the regulatory approval of new CFTR modulators, because other possible trial designs will require too many participants. Our results suggest that when new modulators intended for the same patients as Kalydeco® or Orkambi® are studied, placebo-controlled trials will only be feasible if a) patients being recruited don't have access to these modulators or b) if the studies are only run for short (4-week) periods. Although survey responses were consistent across different groups, some patient/family groups (for instance, patients taking Kalydeco) did not include very many people.

What's next?

Our results will need to be confirmed in larger surveys and in other geographic regions. If found to be correct, drug developers and regulators will need to work together to design shorter placebo-controlled trials for studying newer CFTR modulators for these patients.

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