**Title:** Evaluation of the drug interaction between rifabutin and elexacaftor/tezacaftor/ivacaftor (ETI)

**Lay Title:** Studying the impact of rifabutin on elexacaftor/tezacaftor/ivacaftor (ETI) treatment in cystic fibrosis

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**What was your research question?**

Can rifabutin, an antibiotic sometimes used to treat difficult lung infections, be safely given with the cystic fibrosis (CF) medicine elexacaftor/tezacaftor/ivacaftor (ETI, also known as Trikafta®) without reducing its effectiveness?

**Why is this important?**

People with CF are now living longer because of ETI, but some also develop infections with bacteria called nontuberculous mycobacteria (NTM). These infections are difficult to treat and require long courses of multiple antibiotics. Rifampin, a common antibiotic, cannot be used with ETI because it reduces ETI levels too much. Rifabutin may be a safer alternative, but we need to understand its effects on ETI in the body. Having more antibiotic options available is important so people with CF can receive effective treatment for both their underlying disease and difficult infections.

**What did you do?**

We studied six healthy adults who each received a single dose of ETI. After allowing the drug to clear from their bodies, they then took rifabutin daily for two weeks before receiving another ETI dose. We compared how much ETI was present in the body when taken alone versus when taken with rifabutin.

**What did you find?**

When ETI was taken with rifabutin, its levels in the blood were reduced, but not as much as when ETI is combined with rifampin. Computer models suggest that even at these lower levels, ETI may still remain effective.

**What does this mean, and reasons for caution?**

Our findings suggest rifabutin could potentially be used with ETI, offering a treatment option for CF patients who develop difficult NTM infections. However, our study was small and only included healthy volunteers, not people with CF. The effect of rifabutin on ETI may vary between individuals, and more research is needed in people with CF to better understand long-term safety, effectiveness, and whether dose adjustments are necessary.

**What’s next?**

While our study findings are encouraging, larger clinical studies in people with CF are needed to confirm whether rifabutin can be safely and effectively used alongside ETI for treating NTM infections.

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