

The impact of CFTR modulators on bone health

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Abstract

We are hopeful that CFTR modulation does have a positive impact of bone health, but we have concerns about this study design being used to support the hypothesis.

To the Editor,

We saw with interest the paper by Gur et al reporting the effect of Trikafta (elxacaftor/ivacaftor/tezacaftor) on bone density in young adults with cystic fibrosis. This is an area of significant need in terms of research, and we are glad that it is being considered. However, we would like to raise a number of questions regarding the findings.

The small size of the study (8 patients had 2 DEXA scans) we acknowledge is not unusual in a pilot study, although it is difficult to draw any conclusions from such a small group.

The lack of information regarding the control group is of significant concern. No demographic or DEXA data is offered for the control group.

An increase in bone density over 2 years in an 18yr old would be normal. It is unclear whether the control group are age-matched, which would have a big impact on these findings. It is unclear whether genotype matching with the controls could have been achieved; it seems probable that as patients not receiving Trikafta the control group represent non-eligible genotypes which would also have impact on disease trajectory. A number of other features could be matched: weight and height at time of entering the study, diabetes status, lung function, pubertal stage, vitamin D status. These all have a significant impact and are not mentioned within the study design or discussion. The only place corticosteroids are mentioned are in the case of participant 4, who had a reduction in bone mineral density despite Trikafta.

The DEXA scans are 2 years apart, but Trikafta was given for only 3 months of this. It seems likely that most of the improvement in bone density happened prior to the commencement of Trikafta given the timeframes. The effect of both growth and weight gain within this timeframe should not be overlooked.

We are hopeful that CFTR modulation does have a positive impact of bone health, but we have concerns about this study design being used to support the hypothesis.

Yours sincerely

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