Cystic Fibrosis Research News

Title:

Elexacaftor/Tezacaftor/Ivacaftor Improves Chronic Rhinosinusitis Detected by Magnetic Resonance Imaging in Children with Cystic Fibrosis on Long-Term Therapy with Lumacaftor/Ivacaftor

Lay Title:

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What was your research question?

Elexacaftor/Tezacaftor/Ivacaftor (ELX/TEZ/IVA) therapy was previously approved in Europe for treatment of children (≥6 years) with cystic fibrosis (CF). This therapy was shown to improve symptoms of chronic rhinosinusitis (CRS) in CF. The aim was to assess the effects of ELX/TEZ/IVA on paranasal sinus manifestations detected by magnetic resonance imaging (MRI).

Why is this important?

CRS can cause symptoms such as headache and anosmia, and can trigger pulmonary infections. It was previously shown that MRI is a non-radiative, non-invasive imaging technique to depict and differentiate CF-typical paranasal sinus abnormalities. Moreover, it was shown that CRS improves in adults treated with ELX/TEZ/IVA. But it was still unclear which abnormalities and to which extend the CRS detected by MRI can improve in school-aged children under the novel therapy. The MRI could therefore be a useful imaging tool for the follow-up of CRS during therapy already in young patients.

What did you do?

30 children with CF with at least one F508del mutation underwent three longitudinal paranasal sinus MRI examinations. The first MRI was performed before any cystic fibrosis transmembrane conductance regulator (CFTR) modulator therapy (MRI1), the second MRI without (number of patients = 16) or with Lumacaftor/Ivacaftor (LUM/IVA) therapy (number of patients = 14, MRI2), and the third MRI under ELX/TEZ/IVA therapy (MRI3, age at therapy initiation between 6 and 16 years). All MRI were evaluated using a previously established MRI scoring system for chronic rhinosinusitis (CRS-MRI score).

What did you find?

We demonstrated that the CRS-MRI score remains stable in the absence of a CFTR modulator therapy and under LUM/IVA therapy in preschool and school-age children with CF. But after first therapy with ELX/TEZ/IVA the maxillary sinus deformation decreased and the prevalence, dominance and severity of CRS in school-aged children with CF improved. Importantly, mucopyoceles were improved. The improvements are also shown by a reduction of the CRS-MRI sum score.

Moreover, our study showed that the decrease in the CRS-MRI score was similar in CFTR modulator naïve children with CF and in children with CF pretreated with LUM/IVA.

What does this mean and reasons for caution?

Our study demonstrates improvements in the CRS-MRI score after therapy initiation with ELX/TEZ/IVA in school-aged children with CF. The improvements were independent of a previous LUM/IVA therapy. The observed additional benefit in response to ELX/TEZ/IVA demonstrates a higher effectiveness of ELX/TEZ/IVA compared to LUM/IVA on CRS.
Our results support the use of paranasal sinus MRI as a sensitive radiation-free tool for the detection of response to therapy of CF-related abnormalities of the upper airways.
Unfortunately, we did not obtain a CRS symptom score to systematically assess the relation between the paranasal sinus abnormalities detected by MRI and clinical disease burden.

What's next?

Since ELX/TEZ/IVA is now approved for children aged 2 years and older the effects of early therapy initiation with ELX/TEZ/IVA should be obtained. Moreover, longitudinal effects of ELX/TEZ/IVA on the development of paranasal sinuses and CRS should be studied.

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