Conclusion: We present genotype-phenotype correlations in cis*CFTR*a in three Czech cases where the therapeutic effect of ETI has not been fully pronounced. Long-term follow-up and the sequencing of the entire *CFTR* coding region is necessary to detect and assess the impact of cis*CFTR*a in ETI-CFTRm.

P030

Clinical and genetic characteristics of carriers of complex alleles of the *CFTR* gene

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Introduction: Complex alleles arise from the combination of two or more CFTR variants in cis (i.e., on the same allele), which usually act as pathogenic variants, whereas a single variant may have little or no effect.
Materials and methods: An analysis of medical records of patients with CF with complex *CFTR* alleles observed at the Russian CF Center was carried out. To determine the intestinal current measurement (ICM), biopsy material from the rectum of patients was used. DNA for sequencing was isolated from leukocytes in the venous blood of patients.
Results: A study was conducted using the ICM method in 13 patients: L467F;F508del carriers – 7 people, S466X;R1070Q – 5 people. and E217G;G509D – 1 person, the effectiveness of targeted therapy Elexacaftor + Tezacaftor + Ivacaftor + Ivacaftor (ETI) was assessed in 2 people. In patients carrying complex alleles L467F;F508del (allelic frequency 0.74%), S466X;R1070Q (allelic frequency 0.51%) in a compound heterozygous state with a "severe" variant of the *CFTR* gene, there is a lack of function of the CFTR chloride channel when measuring current density short circuit in response to stimulation with forskolin (ΔI_{SC} 2.27 ± 0.38 μA/cm^2 and 2.33 ± 0.89 μA/cm^2, respectively) and exocrine pancreatic function (pancreatic elastase 1 <200 μg/g feces), a severe course of the disease is noted. Clinically, there is no positive effect from the use of ETI in patients with complex alleles in the genotype (in compound heterozygous carriers with a class I variant); in ICM, restoration of CFTR channel function was not observed.
In a patient carrier E217G;G509D (allelic frequency 0.01%) in a compound heterozygous state with a "severe" variant of the *CFTR* gene, the functional activity of the CFTR chloride channel of epithelial cells is partially preserved (ΔI_{SC} 25 ± 3.37 μA/cm^2), there is preserved exocrine pancreatic function glands (pancreatic elastase 1 >500 mcg/g feces), mild course of the disease. A positive effect (decreased sweat test) was noted from the use of ETI in this patient for 6 months.
Conclusion: Carriers of complex alleles L467F;F508del, S466X;R1070Q are characterized by the absence of exocrine pancreatic function, severe course of the disease, lack of chloride channel function in response to stimulation with forskolin, ETI is not effective, and the complex variant E217G;G509D is characterized by residual function of the CFTR channel and pancreas glands, mild course of the disease, ETI therapy is effective.
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P031

Determining the genotypic and phenotypic characteristics of patients in the Turkish National Cystic Fibrosis Registry System

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Introduction: We aimed to assess the variant results of patients in the Turkish National Cystic Fibrosis Registry System, categorize them according to the CFTR2 and CFTR France databases, and explore genotype-phenotype relationships
Materials and Methods: In 2022, there were 2088 patients in the Registry. Variant results of 1906 patients were reviewed in the CFTR2 and CFTR France databases, patients were divided into 3 groups according to the genetic results: Group 1 those with 2 disease-causing variants, Group 2 those with 1 disease-causing variants in at least one of the databases, and Group 3 those with no variants in both databases.
Results: The percentage of males was 53.1%. The rate of patients was 62.8% in Group 1, 17.4% in Group 2, and 11.9% in Group 3. 248 new variants could not be found in both databases. The age at diagnosis was older in the Group 2 [0.42 (0.17–2.0) years] than the Group 1 [0.33 (0.17–0.75) years](p:0.011). Sweat test values were lower in the Group 3 than in the Group 1 ($p < 0.05$). The FEV1 and FVC percentage values of the Group 3 were lower than the Group 1 ($p < 0.05$). Newborn screening test positivity rate, therapies (hypertonic saline, inhaled antibiotics, rhDNase, ursodeoxycholic acid, pancreatic enzyme, proton pump inhibitör, modulator therapy), the number of pulmonary exacerbations, history of salt loss and liver disease without cirrhosis were detected more frequently in the Group 1 than in the Group 3 ($p < 0.05$). Colonization (*Pseudomonas aeruginosa, Staphylococcus aureus* colonization, nontuberculous mycobacteria growth), the number of antibiotic days and days of hospitalization were detected more frequently in the Group 1 than Group 3 ($p < 0.05$).
Discussion: National registry systems data are useful tools for identifying cystic fibrosis patients with uncommon mutations and assessing the phenotypic and genotypic effects of these mutations. Due to rare mutations, countries can develop their own genotype profiles.