

# DEOXYNUCLEOTIDES dTMP AND dCMP IN THE TREATMENT OF MITOCHONDRIAL MYOPATHY BY MUTATIONS ON THE TK2 GENE

Cifuentes S, Alférez I, Sierra F, Molina E, Verdejo F  
Servicio de Farmacia. Complejo Hospitalario Torrecardenas. Almería.

## Objective

To analyze the deoxynucleotides use in mitochondrial diseases. Syndromes by mtDNA (MDS) depletion embrace very secondary heterogeneous diseases to defects in the mitochondrial respiratory chain. MDS are due to primary defects in nDNA genes that cause secondary defects of the mtDNA. One of these genes is the TK2, which codifies the timidin-kinase (TK2), a necessary mitochondrial enzyme for the phosphorylation of the pyrimidine nucleosides (thymidine and cytidine), giving rise to deoxythymidine monophosphate (dTMP) and deoxycytidine monophosphate (dCMP). Nowadays, there is any effective treatment for mitochondrial diseases.

## Material and Methods

Male of 2 years and 10 months old, who consulted because of progressive weakness and regression of the psychomotor development in evolution. Just at the 8 months from the beginning of the symptoms, the patient was able neither to walk nor to remain standing. It is requested a study about the molecular level of the TK2 gene, identifying two mutations. Presently, in Columbia University, it is achieved to demonstrate a favourable effect on animal models, by utilizing oral administration of the dTMP and dCMP, in a dose of 200mg/Kg/day; which delays the disease progression and duplicates the mice survival. Nowadays, this treatment is already being used on three patients worldwide with positive results.

Application and authorization for compassionate use of these deoxynucleotides, which the patient can not synthesize, as substitutive therapy. Revision of the patient's clinic history from the disease diagnostic to his present situation.

## Results

The patient, after 4 months of treatment, has improved the muscular capacity and head support, and parents refer to an evident clinic improvement.

## Conclusions

On patients with TK2 mutation, are being obtained positive results and absence of secondary effects with the resulting benefit in health and quality of life of the patient through the contribution of deoxynucleotides. Are required prospective studies, well designed, to quantify the possible benefit of these treatments.



CP-008