UCB News

New data on investigational therapy for thymidine kinase 2 deficiency presented at Muscular Dystrophy Association (MDA) 2025 Conference

- Clinical data highlight survival benefits and improvement in functional motor outcomes associated with treatment with doxecitine (dC) and doxribtimine (dT) - an investigational pyrimidine nucleoside therapy - in people living with thymidine kinase 2 deficiency (TK2d).[1,2,3]
- Additional patient experience data emphasize the profound physical challenges and severe psychological strain that come with living with TK2d, and the heavy emotional and physical burden experienced by caregivers.[4,5]
- Across all study populations, pyrimidine nucleoside and/or nucleotide therapy was generally well tolerated. [1,2,3]
- TK2d is an ultra-rare, life-threatening, genetic mitochondrial disease with no currently approved treatment options.[6,7,8,9,10,11]

Brussels (Belgium) 19 March 2025 – 07:00 AM (CET) – UCB, a global biopharmaceutical company, today announced positive data from studies involving its investigational pyrimidine nucleoside therapy, doxecitine (dC) and doxribtimine (dT), in people living with thymidine kinase 2 deficiency (TK2d), at this year's MDA Clinical and Scientific Conference, Dallas, Texas, March 16-19, 2025.

The data show that in individuals with TK2d who were aged 12 years or less when their symptoms first appeared, treatment with pyrimidine nucleoside and/or nucleotide therapy significantly decreased mortality and increased survival.[2,3] In addition, treatment also improved functional outcomes irrespective of age of onset, including retaining or regaining motor milestones, and helped stabilize ventilatory and feeding support use.[1,2,3] Across all study populations, pyrimidine nucleoside and/or nucleotide therapy was generally well tolerated with diarrhea being the most common treatment emergent adverse event. [1,2,3]

Thymidine kinase 2 deficiency is an ultra-rare, life-threatening, genetic mitochondrial disease characterized by progressive and severe muscle weakness (myopathy), which can impact the ability to walk, eat, and breathe independently.[6,7,8,9,10]

"There are no approved therapies or international clinical guidelines for the management of TK2d, therefore we are very excited to share this data with the medical community at MDA," said Donatello Crocetta, Chief Medical Officer at UCB. "The data highlight the positive impact this investigational treatment could have on the lives of people living with this debilitating and life-threatening condition."

Data from participants treated in the doxecitine (dC) and doxribtimine (dT) clinical program were pooled from retrospective and prospective sources and a company-supported expanded access program (EAP). Data from untreated participants were pooled from literature reviews of case series and reports, and a retrospective chart review study. Subgroups were stratified by age of TK2d symptom onset categories and reported for participants with age of TK2d symptom onset ≤12 years and >12 years.

Doxecitine and doxribtimine is currently under regulatory review by US and EU regulatory authorities. The safety and efficacy have not been established, and doxecitine and doxribtimine has not been approved by the US Food and Drug Administration (FDA) nor the European Medicines Agency (EMA).

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Key findings from the studies

Improvement in survival:

- Among people living with TK2d with an age of symptom onset 12 years or less, treatment with nucleoside and/or nucleotide therapy reduced risk of death by 92–94% (hazard ratio=0.06–0.08; $p<0.0001$) and 87–95% (hazard ratio=0.05–0.13; $p<0.0001$) in the time from symptom onset and starting treatment, respectively.[3]

Enhanced functional outcomes:

- Among people living with TK2d who were aged 12 years or less when their symptoms first appeared, following treatment with pyrimidine nucleoside and/or nucleotide therapy, 75.0% (30/40) regained at least one previously lost motor milestone, with 22.5% (9/40) regaining four or more motor milestones.[2]
- In addition, ventilatory support dependency decreased, with 16.1% (5/31) of patients reducing usage time and 16.1% (5/31) discontinuing ventilatory support altogether after treatment.[2]

Safety profile:

- Across all study populations, pyrimidine nucleoside and/or nucleotide therapy was generally well tolerated. Diarrhea (range from 84.6%-90.9%) was the most reported treatment-emergent adverse event.[1,2,3]

Impact on quality of life on individuals and caregivers:

- In addition to the data presented on nucleoside and/or nucleotide therapy, patient experience data presented highlight the debilitating physical impacts and severe psychological strain associated with living with TK2d, as well as its impact on caregivers. Many individuals reported the 'extreme' impact the condition has on their quality of life including walking, breathing and eating/swallowing difficulties. Caregivers reported that the constant demands of caregiving and minimal support/respite caused persistent stress and emotional burnout. [4,5]

Key data presented at MDA

Author	Title	Details
Hirano M, et al.	Survival Analyses in Patients with Thymidine Kinase 2 Deficiency Aged ≤12 Years at Symptom Onset Who Received Pyrimidine Nucleos(t)ide Therapy	Assessed survival and safety in patients with an age of TK2d symptom onset ≤12 years who received pyrimidine nucleoside and/or nucleotide therapy. Treated patients were pooled from retrospective (NCT03701568, NCT05017818) and prospective (NCT03845712) sources and a company-supported expanded access program (EAP); untreated patients were pooled from literature reviews of case series and reports and a retrospective chart review (NCT05017818).
Garone C, et al.	Functional Outcomes in Patients with Thymidine Kinase 2 Deficiency Aged ≤12 Years at Symptom Onset Who Received Pyrimidine Nucleos(t)ide Therapy	Assessed functional outcomes and safety in patients with an age of TK2d symptom onset ≤12 years who received pyrimidine nucleoside and/or nucleotide therapy. Treated patients were pooled from retrospective (NCT03701568, NCT05017818) and prospective (NCT03845712) sources and a company-supported expanded access program (EAP; functional outcome data not collected).
Scaglia F, et al.	Survival and Functional Outcomes in Patients with Thymidine Kinase 2 Deficiency Aged >12 Years at Symptom Onset Who Received Pyrimidine Nucleos(t)ides	Assessed survival, functional outcomes and safety in patients with an age of TK2d symptom onset >12 years who received pyrimidine nucleoside and/or nucleotide therapy. Treated patients were pooled from retrospective (NCT03701568, NCT05017818) and prospective (NCT03845712) sources and a company-supported expanded access program (EAP).

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Yeske P, et al.	Patients' Lived Experience of Thymidine Kinase 2 Deficiency (TK2d): Results from the Assessment of TK2d Patient Perspectives (ATP) Study	Individuals with genetically confirmed TK2d (or proxy caregivers) were invited to complete an online mixed-methods survey co-created by a patient steering committee.
Yeske P, et al.	Burden and Impact of Caring for those with Thymidine Kinase 2 Deficiency (TK2d): Results from the Assessment of TK2d Patient Perspectives (ATP) Study	Caregivers of patients with genetically confirmed TK2d were invited to complete an online mixed-methods survey. The survey comprised multiple-choice and open-text questions exploring caregivers' experiences and how caregiving affects their quality of life.

About thymidine kinase 2 deficiency (TK2d)

Thymidine kinase 2 deficiency is an ultra-rare, life-threatening, genetic mitochondrial disease characterized by progressive and severe muscle weakness (myopathy), which can impact the ability to walk, eat, and breathe independently.[6,7,8,9,10] It is estimated that the worldwide prevalence of TK2d is 1.64 [0.5, 3.1] cases per 1,000,000 people.[12] The age of TK2d symptom onset is categorized as ≤12 years and >12 years.[6,7,8]

TK2d profoundly affects multiple health, physical, quality-of-life, and psychosocial domains, as children struggle to achieve developmental milestones or lose them, and adults lose functional independence with challenges in breathing, eating, and walking.[11,13]

About doxecitine and doxribtimine

Doxecitine and doxribtimine is a nucleoside therapy that supports mitochondrial DNA replication resulting in increased or stabilized mitochondrial function in patients with TK2d. Pre-clinical data suggest the primary mechanism of action of doxecitine and doxribtimine is the incorporation of nucleosides deoxycytidine (dC) and deoxythymidine (dT) into skeletal muscle mitochondrial deoxyribonucleic acid (mtDNA), which has the potential to restore mitochondrial DNA copy number and improve skeletal muscle function in patients with TK2d.[14,15,16]

In the U.S., the application has been granted a priority review, Breakthrough Therapy Designation and Rare Pediatric Disease Designation.[17,18]

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About UCB
UCB, Brussels, Belgium (www.ucb.com) is a global biopharmaceutical company focused on the discovery and development of innovative medicines and solutions to transform the lives of people living with severe diseases of the immune system or of the central nervous system. With more than 9000 people in approximately 40 countries, the company generated revenue of € 6.1 billion in 2024. UCB is listed on Euronext Brussels (symbol: UCB). Follow us on Twitter: @UCB_news

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