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H3K27-altered diffuse midline glioma: A paradigm shifting opportunity in direct delivery of targeted therapeutics

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Abstract

Introduction: Despite much progress, the prognosis for H3K27-altered diffuse midline glioma (DMG), previously known as diffuse intrinsic pontine glioma when located in the brainstem, remains dark and dismal.

Areas covered: A wealth of research over the past decade has revolutionized our understanding of the molecular basis of DMG, revealing potential targetable vulnerabilities for treatment of this lethal childhood cancer. However, obstacles to successful clinical implementation of novel therapies remain, including effective delivery across the blood-brain barrier (BBB) to the tumor site. Here, we review relevant literature and clinical trials and discuss direct drug delivery via convection-enhanced delivery (CED) as a promising treatment modality for DMG. We outline a comprehensive molecular, pharmacological, and procedural approach that may offer hope for afflicted patients and their families.

Expert opinion: Challenges remain in successful drug delivery to DMG. While CED and other techniques offer a chance to bypass the BBB, the variables influencing successful intratumoral targeting are numerous and complex. We discuss these variables and potential solutions that could lead to the successful clinical implementation of preclinically promising therapeutic agents.

Keywords: Diffuse midline glioma; H3 K27-altered; H3 K27M; blood-brain barrier; convection-enhanced delivery; diffuse intrinsic pontine glioma; pharmacokinetics; targeted therapeutics.

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