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MEETING ABSTRACT

A1.3

Assessment of regional blood–brain barrier integrity and cerebral efflux transporter function in patients with neuroepithelial tumors using [^{11}C]tariquidar PET

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Background: At the human blood–brain barrier (BBB) high levels of efflux transporters, such as P-glycoprotein (ABCB1) and breast cancer resistance protein (ABCG2), are expressed, which restrict the brain distribution of many different drugs. The pharmacological treatment of brain tumors is often hampered by the impermeability of the BBB to anticancer drugs. It has been shown that the BBB may become disrupted in central necrotic parts of high-grade gliomas, leading to higher anticancer drug concentrations as compared to tumor-free brain tissue. However, little is known to which extent a BBB disruption exists in low-grade glioma. [^{11}C]Tariquidar is a small, drug-like radiotracer, which is subject to efflux transport by ABCB1 and ABCG2 at the human BBB. We used positron emission tomography (PET) with [^{11}C]tariquidar to study regional BBB integrity and cerebral efflux transporter function in patients with neuro-epithelial tumors of the central nervous system.

Methods: Seven patients diagnosed with a neuroepithelial tumor of the central nervous system (WHO I–III) and elected for neurosurgery underwent a 60-min dynamic [^{11}C]tariquidar brain PET scan and simultaneous arterial blood sampling. Four regions of interest (tumor, tumor rim, contralateral as well as ipsilateral tumor-free brain area) were delineated on MR-co-registered PET images. Logan graphical analysis was used to estimate the total distribution volume (V_T) as a parameter of [^{11}C]tariquidar distribution from blood to different brain regions.

Results: In all patients, brain distribution of [^{11}C]tariquidar was very low, which was consistent with ABCB1/ABCG2-mediated efflux transport at the BBB. There were no significant differences in [^{11}C]tariquidar V_T values between tumor tissue and tumor-free tissue and between the central part of the tumor and the tumor rim. In 4 patients, V_T values were lower in tumor tissue as compared to contralateral tumor-free brain tissue (−89 ± 78%, range: −22% to −200%). In 3 patients, V_T values were higher in tumor tissue as compared with contralateral tumor-free brain tissue (+27 ± 14%, range: +13% to +40%).

Discussion: We found no significant differences in distribution of [^{11}C]tariquidar to tumor tissue and tumor-free tissue, which argues against a major BBB disruption in these patients and suggests that anticancer drugs which are transported by ABCB1 and ABCG2, such as tyrosine kinase inhibitors, may not reach the tumor tissue in sufficiently high and therapeutically effective concentrations.

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