Safety assessment of central nervous system tumors in 2-year rat carcinogenicity studies

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Rodent in vivo carcinogenicity bioassays are required for human risk assessment and have been utilized in this capacity for decades. Accordingly, there is an abundance of data that could be accessed and analyzed to better understand the translatability of xenobiotic-induced rodent tumors to human risk assessment. In the past decade various groups have studied and published their assessment of the value garnered by these very lengthy and costly studies. The Expert Working Group (ICH-S1 EWG) was initiated in 2012 to evaluate the predictability of the current testing paradigm and to propose a more comprehensive and integrated approach to human carcinogenicity risk assessment. Results and recommendations by this working group are pending. Key to this effort is the translation of rodent carcinogenicity findings to humans. Some tumors were shown to be rat-specific based on mechanism of action, while others with insufficient evidence remain of potential risk to human. CNS tumors in the rat are very rare and translatability to human remains unknown. This presentation focuses on one type of CNS tumor (microglial cell tumor [MCT]) which is observed specifically in male rats that were exposed to a few pharmaceutical drugs and discusses the classification, nomenclature, potential mechanism of action of this type of CNS tumor, and speculates about its relevance to human.