

DNA REPAIR MECHANISMS AS TARGETS FOR THERAPY OF PITUITARY ADENOMAS

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Edward R. Laws, MD, a neurosurgeon at Brigham and Women's Hospital and director of the Pituitary and Neuroendocrine Center, successfully completed a temozolomide (TMZ) trial with the support from the Daniel E. Ponton Fund. TMZ, a chemotherapy agent, has been effective in treating glioblastomas, the most malignant type of brain tumor. In a clinical trial surveying seven patients with aggressive pituitary tumors, Dr. Laws was able to demonstrate conclusively that TMZ, a chemotherapy agent, works effectively for patients with these often deadly variants of aggressive and malignant pituitary tumors for which prior therapies, both chemo and radiation, have proven to be completely ineffective.

“We studied the positive response of TMZ for aggressive and malignant pituitary tumors, and it resulted in dramatic shrinking of many of the tumors. We further examined the patients who responded to the drug and discovered that the patients who responded to the drug do not have inactivation of an enzyme called MGMT,” says Dr. Laws. “We wanted to investigate whether the patients with a pituitary tumor show the same activation status of this enzyme as that seen in responsive GBMs.”

Dr. Laws's research team then used both precise molecular biology and also a qualitative method of staining the tissue to measure the activity of the enzyme. “Our research showed that there is no correlation between the inactivation of MGMT and the effect of the drug in pituitary patients,” says Dr. Laws. “We also found that none of our patients have an inactivation of the enzyme. The result is beautiful: Five out of seven patients showed a positive response to the drug, independent of activation or inactivation of MGMT.”

Even with just seven patients, the findings were conclusive. The drug can now be administered to patients with aggressive pituitary tumors. “It is highly unusual for a small patient population to reach such a comprehensive result. “Our research, however, clearly demonstrated that TMZ works for most of these patients with this very difficult type of tumor. The other good news is that the side effects are tolerable,” says Dr. Laws, while adding that long-term effects are still unknown because treatment with TMZ just started within the past few years.

The research shows that the preliminary testing with staining is unnecessary. “To show that the staining method is completely unreliable for patients with pituitary tumors saves money for both patients and the healthcare administration,” says Dr. Laws pointing out that the pituitary tumors respond differently to TMZ from glioblastomas.

“We rarely see a research project as black and white as this one. We came up with a definite conclusion that allowed us to administer the drug before we finished examining all the patients signed up for the trial. In addition, we were able to trim healthcare costs.”