

## In Reply: A Clinical Rule for Preoperative Prediction of BRAF Mutation Status in Craniopharyngiomas

To the Editor:

We thank the authors for their comment<sup>1</sup> on our article, “A Clinical Rule for Preoperative Prediction of BRAF Mutation Status in Craniopharyngiomas.”<sup>2</sup> We appreciate their detailed investigation highlighting correlations among pathological, surgical, and radiological findings from the preoperative magnetic resonance imaging.

The authors describe a logistic regression model using such variables as “distortion of the anatomical structures constituting the hypothalamic-pituitary axis,” “mamillary body angle,” and “tumor topography, shape, and consistency” to predict craniopharyngioma histology. While the model achieves a gratifying degree of correct classification, the applicability of their results to other centers – in the end, the true test of whether a classification scheme is useful – also rests on inter-rater reliability, which is not shown here. Indeed, as pointed out by the authors, we declined to use a “tumor consistency” variable because this descriptor failed to show adequate inter-rater reliability in our hands.

A significant advance in surgical oncology elsewhere in the body has been the introduction of neoadjuvant chemotherapy. Particularly in locations where important functions depend on structural integrity of normal tissues, reducing the volume of tumor that must be excised can make all the difference in post-treatment quality of life. This is why neoadjuvant chemotherapy is now the standard of care for many chemosensitive tumors in locations such as the oral cavity, larynx, esophagus, and rectum, as well as for some sarcomas, allowing preservation of key joints and even limb salvage.

Studies have shown that many, perhaps most, patients with craniopharyngioma may achieve good tumor control, but fail to return to work or school. Pereira et al reported that 57% were unable to return to work or school despite 82% achieving a “cure.”<sup>3</sup> In addition, a recent study has shown that craniopharyngioma resection is frequently associated with postoperative neuropsychological deterioration and impaired quality of life.<sup>4</sup> All can agree that these results need further improvement.

While the safety and efficacy of adjuvant chemotherapy for papillary craniopharyngiomas is being actively tested,<sup>5</sup> it is not yet clear that this modality will enter routine clinical practice, or where in the sequence of treatments it will be best employed.

However, now is the time for investigators to develop noninvasive or minimally invasive methods of reliable diagnosis of papillary craniopharyngiomas that are portable across the spectrum of clinical practice against the day this valuable treatment is ready for use.

### Disclosures

Dr Cahill has received consultant fees from Lilly and travel fees from Merck. Dr Brastianos has received consultant fees from Tesaro, Angiochem, Genentech-Roche, and Lilly, Speaker's Honoraria from Merck and Genentech-Roche, and research support (to MGH) from Merck and BMS. The authors have no personal, financial, or institutional interest in any of the drugs, materials, or devices described in this article.

**Shingo Fujio, MD, PhD\*‡**

**Tareq A. Juratli, MD\*‡**

**Daniel P. Cahill, MD, PhD‡**

**Fred G. Barker II, MD‡**

**Priscilla K. Brastianos, MD\***

\*Divisions of Neuro-Oncology and Hematology/Oncology  
Departments of Medicine and Neurology  
Massachusetts General Hospital Cancer Center  
Harvard Medical School  
Boston, Massachusetts

‡Department of Neurosurgery  
Massachusetts General Hospital  
Harvard Medical School  
Boston, Massachusetts

### REFERENCES

- Prieto R, Pascual JM, Barrios L. Letter: a clinical rule for preoperative prediction of BRAF mutation status in craniopharyngiomas. *Neurosurgery*. 2019;85(5):E962-E965.
- Fujio S, Juratli TA, Arita K, et al. A clinical rule for preoperative prediction of BRAF mutation status in craniopharyngiomas. *Neurosurgery*. 2019;85(2):204-210.
- Pereira AM, Schmid EM, Schutte PJ, et al. High prevalence of long-term cardiovascular, neurological and psychosocial morbidity after treatment for craniopharyngioma. *Clin Endocrinol*. 2005;62(2):197-204.
- Giese H, Haenig B, Haenig A, Unterberg A, Zweckberger K. Neurological and neuropsychological outcome after resection of craniopharyngiomas. *J Neurosurg*. 2019;19:1-10. (doi: 10.3171/2018.10.JNS181557).
- Juratli TA, Jones PS, Wang N, et al. Targeted treatment of papillary craniopharyngiomas harboring BRAF V600E mutations. *Cancer*. published online: 2019. (doi: 10.1002/cncr.32197).

10.1093/neuros/nyz327