Germline and somatic mutations in uveal melanomas recurring after eye preserving local treatments

---

Posterboard#: A0110

Abstract Number: 2256 - A0110

AuthorBlock: *Mohamed H. Abdel-Rahman[1,2], Peter Johansson[3], Maha Hussein[1], Lindsey Byrne[2], Frederick H. Davidorf[1], Nicholas Hayward[3], Colleen M. Cebulla[1]*

[1]Ophthalmology and Visual Sciences, The Ohio State University Wexner Medical Center, Columbus, Ohio, United States; [2]Division of Human Genetics, Department of Internal Medicine, The Ohio State University Wexner Medical Center, Columbus, Ohio, United States; [3]QIMR Berghofer Medical Research Institute, Herston, Queensland, Australia;

DisclosureBlock: Mohamed H. Abdel-Rahman, None; Peter Johansson, None; Maha Hussein, None; Lindsey Byrne, None; Frederick H. Davidorf, None; Nicholas Hayward, None; Colleen M. Cebulla, None;

Purpose

The aim of this study was to identify germline and somatic mutations in cancer genes in uveal melanoma (UM) patients with recurrence of the tumor after primary eye conservation therapy including radiation and transpupillary thermotherapy (TTT).

Methods

A retrospective IRB approved cross-sectional study of UM cases with enucleation after tumor recurrence. Eight patients were identified, two with recurrence after TTT and 6 with recurrence after irradiation. Whole exome sequencing (WES) was carried out on matching germline and tumor samples.

Results

Actionable germline pathogenic variants were identified in two cases, one in MSH6 and the other in FAP. One patient had family history of UM. He had recurrence of the lesion, but reevaluation indicated two separate primary UM. This patient had a germline pathogenic variant in the MMS19 DNA damage repair gene as well as germline likely pathogenic variant in ATAD5, which is another DNA damage repair gene. None of the tumors had the UV mutation signature. The most common tumor mutation signature was SB39 (3/8 cases). Other mutations signatures were observed in only one case each. All eight tumors had GNAQ/11 mutations, one had BAP1, two had SF3B1, two had EIF1AX. Two tumors had Chr3p loss with 4 additional ones with Chr3q loss. Seven tumors had Chr6p gain, 5 had Chr8q gains. Two of the patients had personal history of skin melanomas. The tumor mutation burden in the TTT treated tumors were 2-3-fold higher than those treated with irradiation.

Conclusions

Patients with recurrent UM tumors after primary therapy could have germline mutations in DNA repair genes that predispose them to recurrence. The mutation burden in tumors treated with TTT is higher than in those treated with radiation, this should be further investigated.