



Retinoic acid for treatment of glioma patients

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Introduction

Mutation in isocitrate dehydrogenase 1 (IDH1) is present in a large percentage of gliomas and is associated with improved patient survival. Retinoic acid treatment with isotretinoin may delay tumor recurrence in malignant gliomas; however, its survival benefit remains controversial. This study aims to evaluate the effects of isotretinoin in patient with diffuse gliomas.

Methods

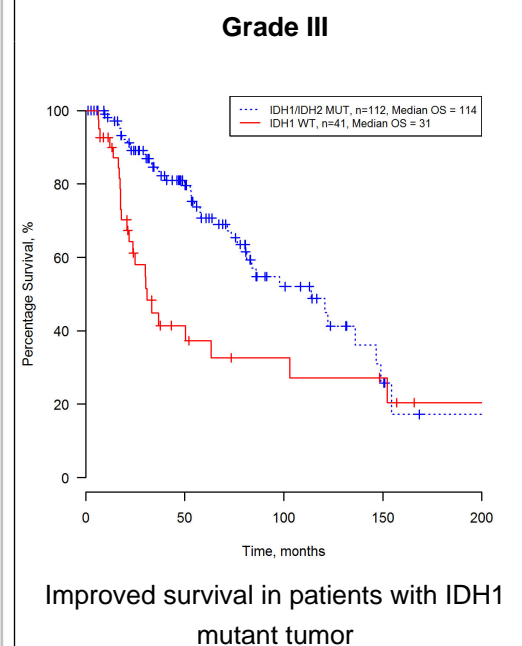
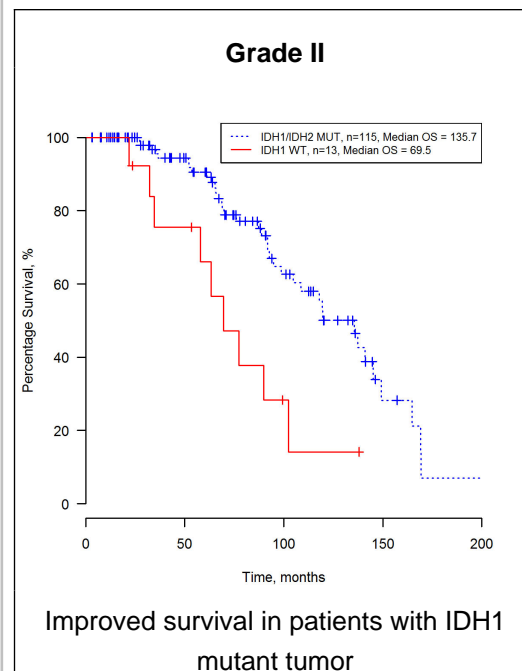
We retrospectively identified glioma patients treated at UCLA and collaborating institutions. Molecular biomarkers including MGMT, IDH1 and IDH2 were evaluated by methylation specific PCR and sequencing, respectively. Overall Survival (OS) was evaluated by Kaplan-Meier analysis and Cox proportional hazard model.

Results

830 patients were evaluated: 128 grade II, 153 grade III, and 549 grade IV patients. Patients with IDH1/IDH2 mutation showed improved OS; Grade II: 135.7 months vs. 69.5 months (mutant vs. wildtype, n=115 and n=13, p=.002); Grade III: 114 months vs. 31 months (n=112 and n=41, p=.002); and Grade IV: 36.1 months vs. 17.9 months (n=69 and n=480, p<.001). Treatment with isotretinoin upfront is associated with an increased median OS in grade IV IDH1 wildtype patients from 17 months to 20.3 months (n=302, non-isotretinoin vs. n=117, isotretinoin, p<.001, Cox models HR=1.47, p=.006).

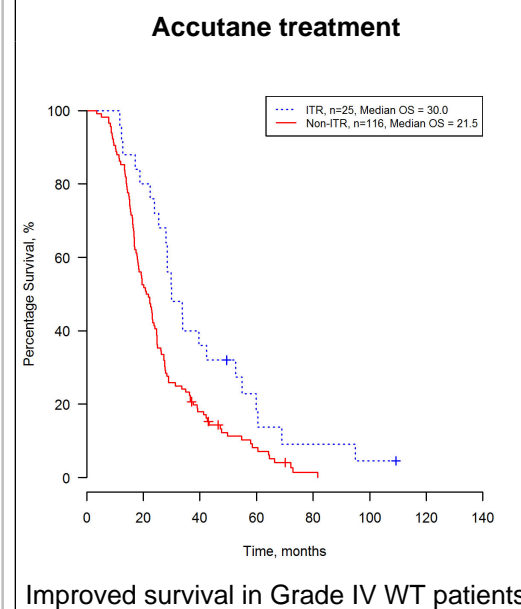
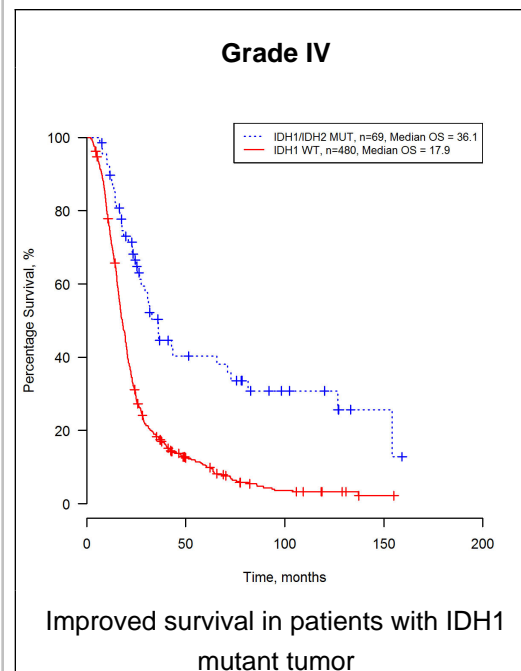
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Learning Objectives

The proposed abstract demonstrates that mutations in the isocitrate dehydrogenase genes (IDH1/IDH2) are associated with significantly improved overall survival in grade II-IV glioma patients. Treatments with isotretinoin appeared to have an impact on overall survival but this association was only observed in patients with grade IV IDH1 wild-type tumors.

Conclusions

IDH1/IDH2 mutation is associated with longer OS in gliomas. Treatment with isotretinoin upfront is associated with longer survival in patients with grade IV IDH1 wildtype tumors. The etiology of this association is unclear. Additional studies are needed to determine if isotretinoin treatment improves OS in other glioma patients.

References

Chou AP, Chowdhury R, Li S, Chen W, Kim AJ, Piccioni DE, Selfridge JM, Mody RR, Chang S, Lalezari S, Lin J, Sanchez DE, Wilson RW, Garrett MC, Harry B, Mottahedeh J, Nghiemphu PL, Kornblum HI, Mischel PS, Prins RM, Yong WH, Cloughesy T, Nelson SF, Liau LM, Lai A. Identification of retinol binding protein 1 promoter hypermethylation in isocitrate dehydrogenase 1 and 2 mutant gliomas. *J Natl Cancer Inst.* 2012 Oct 3;104(19):1458-69.

Acknowledgment

This work is supported by the CNS Penfield Fellowship, AANS NREF Fellowship, American Brain Tumor Association Basic Research Fellowship Supported by Mr. & Mrs. William L. Jackson in Honor of Bruce