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33 TERT EXPRESSION PREDICTS PROGRESSION-FREE SURVIVAL IN MENINGIOMAS

Chloe Gui*, Justin Z. Wang, Vikas Patil, Alexander P. Landry MD, Pedro Castelo-Branco, Uri Tabori, Kenneth Aldape, Felix Behling, Jill S. Barnholtz-Sloan, Craig Horbinski, Ghazaleh Tabatabai, Andrew Ajisebutu, Jeff Liu, Zeel Patel, Rebeca Yakubov, Ramneet Kaloti, Yosef Ellenbogen, Christopher Wilson, Aaron Cohen-Gadol, Marcos Tatagiba, Eric C. Holland, Andrew E. Sloan, Silky Chotai, Lola B. Chambless, Andrew Gao, Serge Makarenko, Stephen Yip (The International Consortium on Meningiomas (ICOM)), Farshad Nassiri, Gelareh Zadeh; chloe.gui@mail.utoronto.ca

BACKGROUND: TERT promoter mutation (TPM) is a rare but established biomarker in meningiomas associated with aberrant TERT expression and reduced progression-free survival (PFS). While TERT is highly expressed in meningiomas with TPMs, it has also been detected in tumours with wildtype TERT promoters (TP-WT). This study aimed to assess the prevalence of TERT expression and its association with clinical outcome in meningiomas. METHODS: Bulk RNA sequencing (n=604), Sanger sequencing of the TERT promoter (n=1095), and methylation profiling (n=1218) of a multi-institutional cohort of meningiomas (total n=1241) were performed to determine TERT expression, TERT promoter mutation status, and TERT promoter methylation. A cohort of 380 meningiomas from Toronto was used for discovery, and 861 meningioma samples from external institutions were compiled as a validation cohort. RESULTS: TERT expression was significantly higher in meningiomas with TPMs compared to TP-WT. However, TERT was still expressed in 30.4% of meningiomas that lacked TPMs. TERT expression increased with higher WHO grades and was associated with shorter

PFS, even among TP-WT tumours. WHO grade 1 tumours that expressed TERT had PFS similar to those of WHO grade 2, while WHO grade 2 meningiomas expressing TERT had a PFS similar to WHO grade 3 meningiomas. Among grade 3 meningiomas, TP-WT tumoursexpressing TERT had PFS similar to those harbouring TPMs. CONCLUSIONS: TERT expression is associated with reduced PFS in meningiomas, even in the absence of TPMs. Its presence may identify patients at greater risk of progression and should be considered in risk stratification and management strategies.