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17 CHROMOSOME 1P LOSS AND 1Q GAIN ARE HIGHLY PROGNOSTIC AND CAN INFORM WHO GRADING OF MENINGIOMA

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The CNS WHO grade of meningioma was updated in 2021 to include rare molecular features, namely homozygous deletions of CDKN2A or CDKN2B and TERT promotor mutations. Previous work including the recent cIMPACT-NOW statement have discussed the potential value of including chromosomal copy number alterations to help refine the current grading system. Objective: To identify chromosomal copy number alterations which could be used to improve the current CNS WHO grading of meningioma. Design: In this cohort study, patients with surgically treated meningioma were followed until recurrence or progression of disease or death. Chromosomal copy number alterations were then correlated with progression-free survival to identify new outcome biomarkers. Results: Using a cohort of 1964 meningiomas, we demonstrated that loss of chromosome 1p in CNS WHO grade 1 meningiomas was associated with significantly worse outcomes compared to cases without loss of 1p (median PFS 5.83 [95% CI 4.36-Inf] vs 34.54 [16.01-Inf] years, log-rank $p < 0.001$). Outcome of patients with CNS WHO grade 1 tumours with loss of chromosome 1p was comparable to CNS WHO grade 2 tumours (median PFS 4.48 [4.09-5.18] years). Combined loss of chromosome 1p and gain of chromosome 1q portended outcomes which were highly concordant with CNS WHO grade 3 cases regardless of initial grade (median PFS 2.23 [1.28-Inf] years for WHO grade 1 and 1.90 [1.23-2.25] years for WHO grade 2, compared to 2.27 [1.68-3.05] years in all WHO grade 3 cases). Conclusions: Our findings highlight a role for cytogenetic profiling in the next iteration of CNS WHO grading, with a specific focus on chromosome 1p loss and 1q gain. We advocate for chromosome 1p loss in addition to 22q loss being added as a criterion for a CNS WHO grade of 2 and addition of 1q gain as a criterion for a CNS WHO grade of 3.