

SURVIVAL BENEFIT FOR INDIVIDUALS WITH CONSTITUTIONAL MISMATCH REPAIR DEFICIENCY SYNDROME AND BRAIN TUMORS WHO UNDERGO SURVEILLANCE PROTOCOL. A REPORT FROM THE INTERNATIONAL REPLICATION REPAIR CONSORTIUM

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Background: Constitutional mismatch repair deficiency syndrome (CMMRD) is a severe cancer predisposition syndrome resulting in early onset central nervous system (CNS) and other cancers. International guidelines for surveillance exist but no study has systematically evaluated the efficacy of this protocol.

Methods: We surveyed all confirmed CMMRD patients in the International Replication Repair Deficiency Consortium. A surveillance protocol consisting of frequent biochemical, endoscopic and imaging (CNS and total body MRI) studies were employed. Survival analyses and efficacy of each method were assessed.

Results: Surveillance data were collected from 105 CMMRD individuals from 41 countries. Of the 193 malignant tumors, CNS malignancies were the most common (44%). The surveillance protocol uncovered 49 asymptomatic tumors including 16 glioblastomas and medulloblastomas.

Five-year overall survival was 89% for tumors discovered by surveillance, and 61% for symptomatic tumors ($p < 0.004$). Similarly, 5-year survival was $82 \pm 11\%$ and $24 \pm 6\%$ for surveillance and non-surveillance of brain tumors ($p = 0.005$). Yearly total body and q6 month brain MRI detected asymptomatic cancers in all but 3 symptomatic CNS gliomas. These were tumors uncovered when time between scans was > 6 months as per protocol. Finally, of the low grade tumors identified asymptotically, 5 were low grade gliomas. All of the low grade gliomas, which were not resected transformed to high grade tumors at a median of 1.6 ± 0.9 years.

Conclusion: These data support a survival benefit in CMMRD patients undergoing a surveillance protocol. Adherence to protocol and resection of lower grade lesions may improve survival for patients with CNS tumors.