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“NUT” An Anatomical Malignancy! A Solid Tumor Characterized by a Genetic Translocation

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"NUT" An Anatomical Malignancy! A Solid Tumor Characterized by a Genetic Translocation

NUT midline carcinomas are rare poorly differentiated tumors driven by t(15,19) rearrangements and clinically characterized by rapid progression and high mortality.
A 49 year-old-male with no comorbidities, presented with acute worsening of chronic cough, new onset hemoptysis and left sided chest pain for 2 weeks. Workup revealed NUT midline carcinoma of the lung as confirmed by next-generation sequencing that revealed the presence of a NUTM1-BRD4 fusion. He was diagnosed with NUT midline lung cancer clinical stage IIIB. The tumor was not amenable to surgical resection, therefore, he was started on concurrent chemoradiation with weekly carboplatin and paclitaxel for 5 weeks. Follow up CT scan showed partial response and the patient was started on maintenance durvalumab. Two months later, he presented with a metastatic site in the posterior muscle compartment of the left arm and was treated with local radiotherapy (RT). He tolerated maintenance durvalumab until he had pulmonary recurrence four months later. Durvalumab was then stopped, and he was started on BET inhibitor, molibresib 120 mg daily. Nearly 3 months after being on molibresib, he presented with brain metastasis for which he had a craniotomy with tumor resection and gamma knife to solitary metastatic lesions. The patient was then started on chemo-immunotherapy with carboplatin plus pemetrexed and pembrolizumab. After two cycles, his disease progressed and he succumbed to it. The patient survived for a total of 18 months.
An optimal treatment regimen for this rare malignancy has not yet been established. Current treatment approaches are aimed at surgery, chemotherapy and radiation, in varying combinations based upon location and staging. Despite these treatment efforts, remission is generally brief, followed by recurrence of further metastasis, and ultimate mortality.
Data regarding the role of target therapies like bromodomain and extra-terminal domain protein (BET) inhibitors are still in early phases of clinical trials.