Durable response with crizotinib in ROS1 fusion-positive bladder cancer with brain metastases

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The ROS1 fusion represents a druggable target across several malignancies including non-small cell lung cancer. However, ROS1 fusion in bladder cancer is very rare, and its clinical features and treatment outcomes are unknown. Herein, we present the first case of a patient with metastatic ROS1 fusion-positive bladder cancer who showed a long-term response with crizotinib. A 40-year-old Mongolian female visited our hospital on December 2021, complaining of dysuria and dyspepsia that lasted for 2 months. Abdomen and pelvis CT scan showed a 6.8 cm enhancing mass in the urinary bladder causing bilateral hydroureteroneprhosis with multiple lymph nodes and bone metastases. Chest CT and brain MRI showed multiple lung and brain metastases, and serum CEA was elevated to 115 ng/mL. Transurethral resection of bladder was performed and pathology revealed invasive urothelial carcinoma, rhabdoid variant. After two weeks of whole brain radiation therapy, She received two cycles of chemotherapy with gemcitabine and carboplatin. Follow-up CT scan showed no change of tumor burden, but serum CEA increased to 138 ng/mL. The results of Next-generation sequencing (NGS) performed at the time of diagnosis were obtained and CD74-ROS1 fusion was identified. Based on the identification of ROS1 fusion, the patient was started on crizotinib (250mg, orally, once daily), a ROS1, ALK, and MET tyrosine kinase inhibitor (TKI), as a second-line treatment from February 2022. Follow-up CT taken 4 months after treatment with crizotinib showed a reduction in tumor burden in the lungs, LNs and brain, with a partial response according to RECIST 1.1 criteria.(Figure1.) Serum CEA also significantly declined to 1.5ng/mL.(Figure2.) She remained progression-free for 16 months, until June 2023, when brain MRI showed progression of brain metastases. Lorlatinib was recommended as a third-line treatment, but follow-up was discontinued as the patient returned to her home country. In this patient, crizotinib was a well-tolerated treatment with a durable response of 16 months. Comprehensive genomic analysis should be actively accompanied to find potential molecular targets in metastatic bladder cancer.

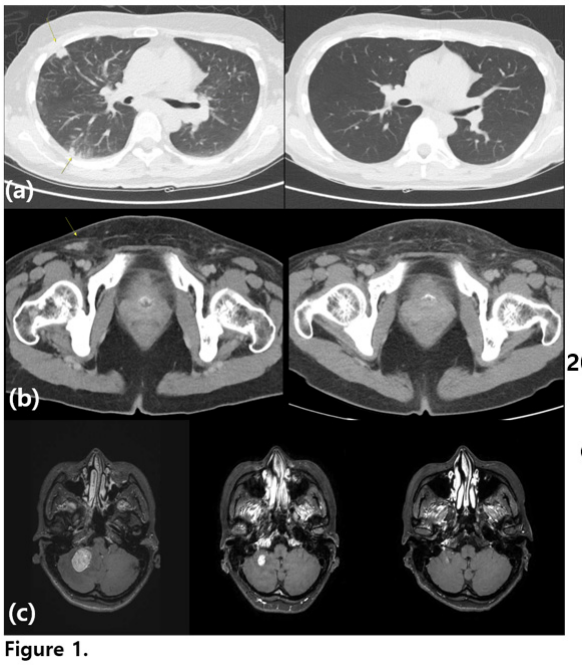

Figure 1.

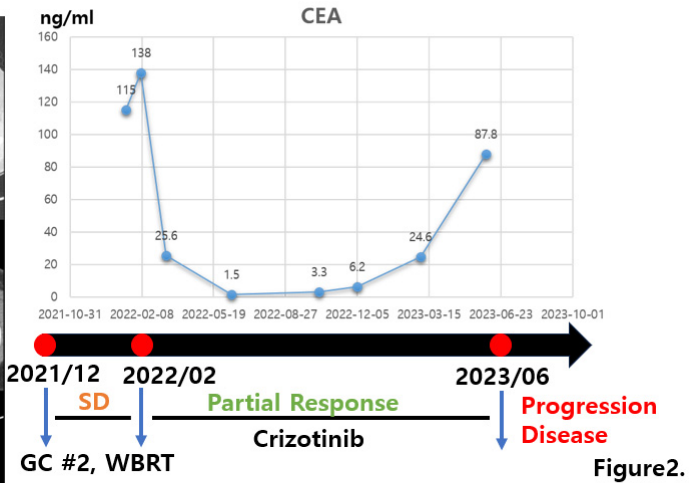

Figure2.

Figure1. Response to crizotinib treatment. Four months of crizotinib treatment revealed decreased tumor burden in lung(a), LNs(b), and brain(c).

Figure2. Change of CEA during crizotinib treatment. Crizotinib demonstrated durable response in ROS1 fusion positive metastatic bladder cancer, and serum CEA significantly declined after crizotinib treatment.