Anaplastic lymphoma kinase (ALK) also known as ALK tyrosine kinase receptor or CD246 (cluster of differentiation 246) is an enzyme that in humans is encoded by the ALK gene.

Anaplastic lymphoma kinase (ALK) was originally discovered in 1994 in anaplastic large cell lymphoma (ALCL) cells.

Currently, the fourth edition of the WHO classification of tumors of hematopoietic and lymphoid tissues, published in 2008, divides systemic Anaplastic large cell lymphomas into two entities: anaplastic lymphoma kinase (ALK)-positive and ALK-negative.

Primary central nervous system ALK-negative anaplastic large cell lymphoma

Primary central nervous system ALK-positive anaplastic large cell lymphoma

ALK-positive large B-cell lymphoma

see ALK inhibitor.

Anaplastic lymphoma kinase (ALK) gene rearrangement was reported in 3%-7% of primary non-small-cell lung cancer (NSCLC) and its presence is commonly associated with adenocarcinoma (AD) type and non-smoking history [1)].

ALK overexpression can be identified in up to 70% of Glioblastomas and does not correlate with underlying alk gene amplification. Despite being more common in rapidly growing, clinically aggressive Glioblastoma, ALK overexpression did not show correlation with prognosis in this study [2)].

Yan et al. studied the expression of anaplastic lymphoma kinase (ALK), a well-characterized tyrosine kinase and drug target, in a cohort of medulloblastomas by immunohistochemistry, and identified three ALK-positive cases. Mutational analyses did not reveal a definite underlying genetic mechanism for the ALK expression, although one of the cases showed an increased ALK copy number. Our findings have clinical implications and warrant further pharmacological and functional studies, as well as evaluation in larger patient cohorts, to fully characterize the value of ALK as a prognostic and predictive therapeutic marker in medulloblastomas [3)].

Anaplastic lymphoma kinase-positive NSCLC patients receiving crizotinib and manifesting ≤ 4 discrete sites of eCNS progression were classified as having oligoprogressive disease (OPD). If subsequent progression met OPD criteria, additional courses of LAT were considered. Crizotinib was continued until eCNS progression was beyond OPD criteria or otherwise not suitable for further LAT. RESULTS: Of 38 patients, 33 progressed while taking crizotinib. Of these, 14 had eCNS progression meeting OPD criteria suitable for radiotherapeutic LAT. Patients with eCNS OPD received 1-3 courses of LAT with radiation therapy. The 6- and 12-month actuarial local lesion control rates with radiation therapy were 100% and 86%, respectively. The 12-month local lesion control rate with single-fraction equivalent

dose >25 Gy versus ≤ 25 Gy was 100% versus 60% (P=.01). No acute or late grade >2 radiation therapy-related toxicities were observed. Median overall time taking crizotinib among those treated with LAT versus those who progressed but were not suitable for LAT was 28 versus 10.1 months, respectively. Patients continuing to take crizotinib for >12 months versus ≤ 12 months had a 2-year overall survival rate of 72% versus 12%, respectively (P<.0001). CONCLUSIONS: Local ablative therapy safely and durably eradicated sites of individual lesion progression in anaplastic lymphoma kinase-positive NSCLC patients receiving crizotinib. A dose-response relationship for local lesion control was observed. The suppression of OPD by LAT in patients taking crizotinib allowed an extended duration of exposure to crizotinib, which was associated with longer overall survival [4].

11-year-old immunocompetent boy with primary CNS CD30-positive anaplastic large-cell lymphoma (ALCL) that was also positive for anaplastic lymphoma kinase-1. His initial clinical manifestation was acute meningitis of unknown etiology. Findings on CT scanning were normal. Although he received empirical treatment against infection, his systemic and neurological status deteriorated. Subsequent MRI revealed newly emerged enhanced lesions and concomitant edema in the left parietal lobe. Diagnosis was confirmed following a brain biopsy and immunohistochemical staining. Three courses of systemic high-dose methotrexate (HD-MTX) treatment with 2-week intervals was started, followed by whole-brain radiation. His clinical course improved, and he has remained disease-free for more than 8 years without any additional treatment. Because ALCL originating in the brain is extremely rare and difficult to diagnose, no standard treatment has been established. This report suggests that systemic HD-MTX monotherapy can be an effective and worthwhile tailored therapeutic option for pediatric primary CNS ALCL [5].

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a 22-year-old man. The patient presented with left lower back pain for 4 weeks. The computed tomography (CT) scan demonstrated an exophytic nodule on the left bladder wall and abdominopelvic lymphadenopathy. Histologically, a population of large pleomorphic cells extensively infiltrated the lamina propria of the bladder. These cells were diffusely and strongly immunoreactive for CD30, ALK, EMA, and vimentin, but were negative for AE1/AE3, CK20, CK7, CK5/6, P63, SMA, HMB-45, pan-Melan, S-100, Myo D1, synaptophysin, CD56, desmin, CD15, CD20, Pax-5, and CD3. Few cells exhibited positive immunohistochemical staining of CD45. The patient underwent cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) regime of chemotherapy and achieved a complete remission after four cycles. This case is the tenth documented case of systemic ALCL involving urinary bladder. Due to its rarity, it is important to be aware of the features of ALCL in bladder, and make prompt and accurate diagnosis [6].

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