中文題目：Crizotinib 在長期臥床的肺癌患者上引起的嚴重食道炎

英文題目：Crizotinib Associated Corrosive Esophagitis in a Bed-ridden Lung Cancer Patient

作　　者：陳怡樺[1,2]，楊志仁[1,2,3,4]

服務單位：高雄市立大同醫院內科部[1]; 高雄市立大同醫院胸腔內科[2] 高雄醫學大學醫學系[3]

Introduction:

Crizotinib is an oral medication that acting as an ALK (anaplastic lymphoma kinase) and ROS1 (c-ros oncogene 1) inhibitor, approved for treatment of non-small cell lung carcinoma (NSCLC). It was shown to possess marked therapeutic efficacy and was approved by the US Food and Drug Administration (FDA) in 2011, now been used worldwide. The major adverse effects of crizotinib are vision disorder, diarrhea, nausea, vomiting, and peripheral edema[1]. However, esophagitis has not been reported as a major crizotinib-related adverse event in large-scale clinical trials. However, several cases of crizotinib associated corrosive esophagitis were reported sporadically since 2013. Herein, we present a stage IV NSCLC woman who developed a severe corrosive esophagitis after 3-week crizotinib treatment in Taiwan.

Case Presentation:

A 80 year-old Chinese woman who has past history with hypertension, presented with skull tumor in the beginning and she underwent cranioplasty and tumor removal. The pathological report disclosed a metastatic adenocarcinoma from lung according to morphology and immunohistochemical staining. In addition, her specimen also showed an immunoreactive to ALK (using D5F3 clone antibody). The patient then started oral Crizotinib 250mg twice daily since Feb 1 2018. In addition, she was a bedridden patient because of lower back pain and lumbar spine metastasis was suspected according to spine MRI. 3 weeks later, She started to complain progressive epigastralgia, odynophagia and retrosternal pain. Esophagogastroduodenoscopy showed diffuse ulcerations with necrosis over her mid- to lower esophagus (Fig 1). The pathological section showed squamous epithelium with ulcer, composed of acute and chronic inflammatory cell infiltration, fibrinous exudate, aggregation of degenerative leukocytes and granulation tissue(Fig 2). No malignancy, fungal or bacterial infection. Finally, crizotinib induced corrosive esophagitis was impressed. We therefore prescribed intravenous pantoprazole and oral Sucralfate but without discontinued crizotinib. Her dysphagia had improved day by day. No more recurrence

of her esophageal symptoms since we prescribed oral Dexlansoprazole and Sucralfate and continued crizotinib

Conclusion:

This is the first case of crizotinib associated corrosive esophagitis in Taiwan.

Till now, There have 8 cases described as Crizotinib related esophagitis been published worldwide[2-9]in Table 1. According to these cases, the common characters include: female(light-weight), patient positioning, and inadequate fluid intake.

Though the etiology of crizotinib associated corrosive esophagitis is still unknown, insufficient water intake and took crizotinib in recumbent position were proposed. Some authors believed the light-weight and low-density capsule of crizotinib is also the possible reason. In addition, the esophagitis always located in the middle third of the esophagus due to external compression of the aortic arch.

In summary, clinicians should be aware that crizotinib may result in severe esophagitis though large scale trials didn't reveal such a life threatening esophagitis. How to prevent this condition is an important issue, adequate fluid intake and remaining upright for a period of time after medication administration are both mandatory to these patient. In addition, oral proton pump inhibitor might take into consideration if patients are in right risks to develop crizotinib associated esophagitis. We believe such a rare but life-threatening ADR is important and timely for these poor lung cancer patients who harbored ALK and took crizotinb for life-saving drug.