

WITH OTHER ANAPLASTIC LYMPHOMA KINASE (ALK)-INHIBITORS

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Background

Anaplastic lymphoma kinase (ALK)-inhibitors are indicated in adult patients with ALK-positive advanced NSCLC, being **crizotinib** indicated as first line. Hepatotoxicity has been described for **crizotinib**^{1,2} and **ceritinib**³.

¹ Van Geel RM, Hendriks JJ, Vahl JE et al. Crizotinib-induced fatal fulminant liver failure. *Lung Cancer* 2016; 93:17-19
² Sato Y, Fujimoto D, Shibata Y et al. Fulminant Hepatitis Following Crizotinib Administration for ALK-positive Non-small-cell Lung Carcinoma. *Jpn J Clin Oncol* 2014; 44:872-5.
³ Product Information ZYKADIA (TM) ceritinib oral capsules. Novartis Pharmaceuticals Corporation, East Hanover, NJ, 2014

Purpose

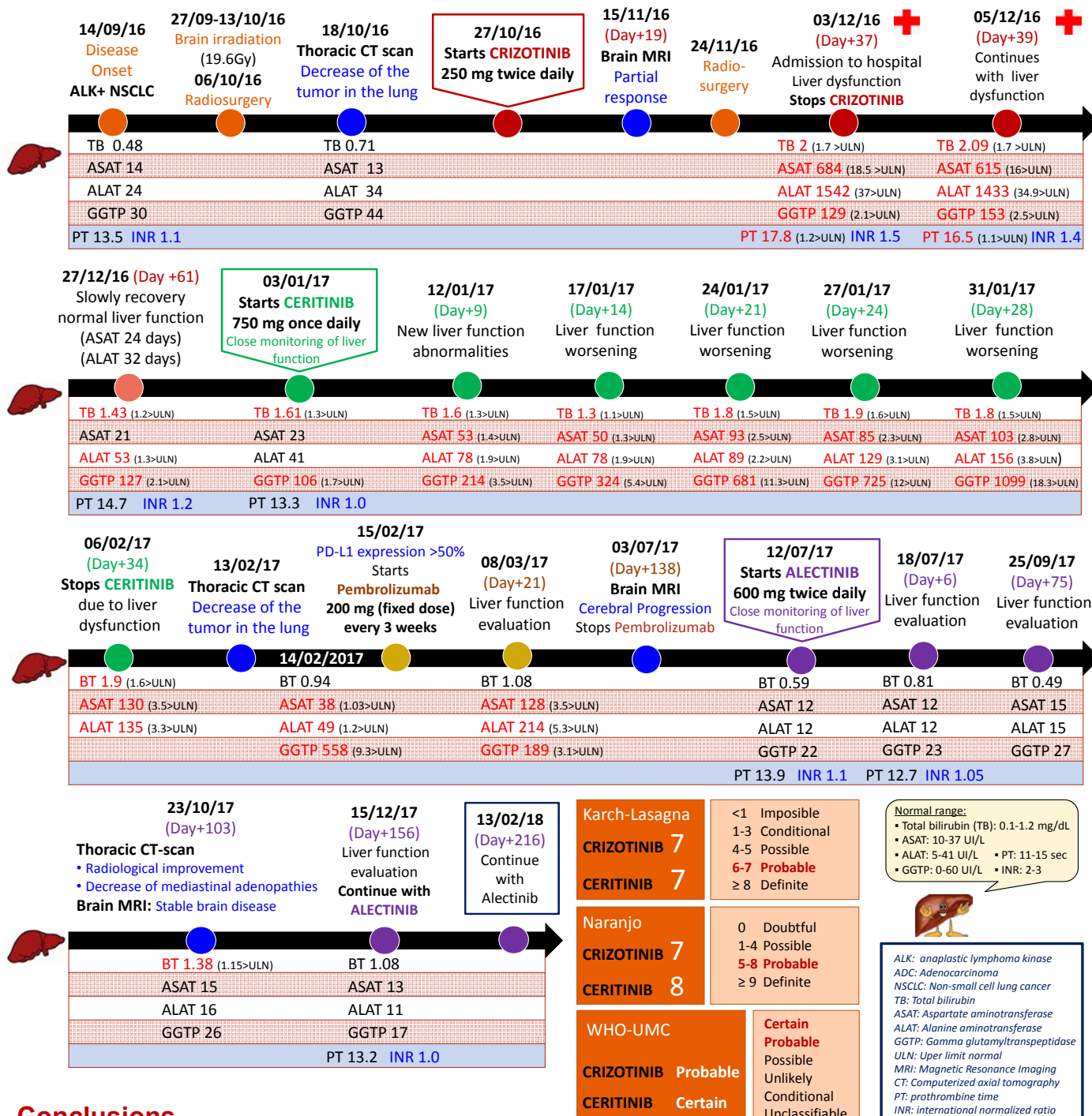
To describe a case of **alectinib** hepatic-tolerance in a patient with hepatotoxicity background with other ALK-inhibitors

Materials & Methods

- ✓ The data were obtained by reviewing the electronic medical records
- ✓ Karch-Lasagna, Naranjo and WHO-UMC algorithms have been used

Results

1. Man
2. 76 years-old
3. **ALK-positive advanced NSCLC**. ADC stage IV (T2aN2M1b)
4. Hypertension
5. Hypercholesterolemia
6. Benign prostatic hyperplasia



Conclusions

- Alectinib may be a therapeutic option in patients with ALK-positive NSCLC who have developed liver toxicity to other ALK-inhibitors. Further follow-up is needed to ratify this statement.
- Karch-Lasagna and Naranjo algorithms established a “probable” relationship between hepatotoxicity and Crizotinib/Ceritinib.
- WHO-UMC algorithm established this relationship as “probable” to crizotinib and “certain” to ceritinib.
- Hepatic toxicity to ALK-inhibitors frequently shows a reversible pattern and transaminases and prothrombine time appear to be the most sensitive markers.

Normal range:

- Total bilirubin (TB): 0.1-1.2 mg/dL
- ASAT: 10-37 U/L
- ALAT: 5-41 U/L
- GGTP: 0-60 U/L
- PT: 11-15 sec
- INR: 2-3

Karch-Lasagna

CRIZOTINIB 7
CERITINIB 7

Naranjo

CRIZOTINIB 7
CERITINIB 8

WHO-UMC

CRIZOTINIB Probable
CERITINIB Certain

0 Doubtful
1-4 Possible
5-8 Probable
≥ 9 Definite

Certain Probable
Possible
Unlikely
Conditional
Unclassifiable

Legend:

ALK: anaplastic lymphoma kinase
 ADC: Adenocarcinoma
 NSCLC: Non-small cell lung cancer
 TB: Total bilirubin
 ASAT: Aspartate aminotransferase
 ALAT: Alanine aminotransferase
 GGTP: Gamma glutamyltransferase
 ULN: Uper limit normal
 MRI: Magnetic Resonance Imaging
 CT: Computerized axial tomography
 PT: prothrombine time
 INR: international normalized ratio