ALK and ROS1-Positive Lung Adenocarcinoma (LA): Patient Outcomes: A Mono-Institutional Experience

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Aim: ALK and ROS1 gene rearrangements are the “oncogenic drivers” of two subsets of LA that have been shown to be sensitive to the ALK inhibitor crizotinib (Criz). We present an observational analysis of the outcome of the ALK and ROS1-positive (pos) patients (pts) treated at our institution.

Methods: We identified 39 ALK-pos LA by analyzing for a 3-gene panel (ALK, KRAS, EGFR) 705 samples. 147 triple-neg samples were studied by FISH for ROS1.

Results: Between September 2011 and April 2014, 46 (39 ALK-pos and 7 ROS1-pos) stage IIIB and IV pts received Criz [n = 47 (100%)] at the dose of 250 mg B.I.D. At progression, 13 pts (28.2%) received ceritinib (Cer) at dose of 750 mg once daily. Criz was administered as 1st line in 2 pts (4.3%), as 2nd-3rd in 34 pts (74.5%) and in subsequent lines in 10 pts (21.3%). Cer was administered as 3rd line in 5 pts (38.5%), as subsequent lines in 8 pts (61.6%). Patients’ characteristics prior to Criz were: 19 (40.4%) males and 28 (59.6%) females. Median age 48 years (range:24-71). 8 pts (17.3%) were current or former smokers while 38 pts (80.9%) never smokers. 40 (85.1%) pts were stage IV and 10 (22.7%) had brain metastases. At start of Criz, ECOG PS was 0-1 in 39 (84.7%) pts and 2-3 in 7 (14.9%) while at start of Cer PS ECOG was 0 for 10 (76.9%) pts and 1 for 3 (23.1%). 100% of pts were evaluable for the activity of both Criz (46/46) and Cer (13/13). The overall response rate (ORR) to Criz was 27/38 (71%) in ALK-pos and 6/7 (85.7%) in ROS1-pos pts. The responses to Criz were: one (2.2%) complete response (CR) in a ROS1-pos pt, 32 (69.6%) partial responses (PR), 7 (15.2%) stable diseases (SD) and 6 (13.0%) progressive diseases (PD) with a median time to response of 2 months. Median progression-free survival (PFS) for Criz was 16.9 months (95% C.I.: 3.6-30.3). While median overall survival (OS) has not been reached, 1- and 2-years OS were of 77% and 72%, respectively. In ALK-pos pts 1- and 2-years OS for Criz were of 74.1% and 69.7%, respectively while in ROS1-pos pts OS was 100% both at 1 and at 2-years. As for Cer, responses were: 10 (76.9%) PR, 2 (15.4%) SD and 1 (7.7%) PD with a median time to response of 1.9 months. Median PFS for Cer was 8.6 months (95% C.I.: 6.3-11.0) and 1- and 2-years OS was 92%.

Conclusions: These data are consistent with those previously reported. In our experience Cer following Criz was associated with a shorter PFS but similar antitumor activity to that seen with Criz.

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