Other RAS mutations incidence in CRCm in routine clinical practice: a center experience.

P-236

Authrs: Beatriz González Astorga¹, Maria Teresa Delgado Ureña¹, Rodrigo López Castro², Encarnación González Flores³ Ana Segura Pérez², Verónica Conde³, Javier García³, Carmen Sánchez-Toro³, ose Miguel Jurado García¹, Ana Villaescusa¹, Fernando Gálvez Montosa¹.

Background: Patients with metastatic colorectal cancer that harbors KRAS mutations in exon 2 do not benefit from anti-epidermal growth factor receptor (EGFR) therapy. Other activating RAS mutations also are negative predictive biomarkers for anti-EGFR therapy, as recently shown in a subanalysis of the PRIME study.

Methods:From June 2013 we began to make the determination of other mutations of RAS. The determination of the mutational status was performed using a validated analytical method for determining KRAS mutations (exons 2, 3 and 4) and NRAS (exons 2,3 and 4) in formalin-fixed, paraffin-embedded specimens. It was used cobas® KRAS mutation test (Roche), which is a real-time PCR test intended for the identification of mutations in codons 12, 13 and 61 of the gene. Pyrosequencing of the NRAS exon 1 (codon 12 and 13), exon 2 (codons 60 and 61) and exon 4 (codon 117 and 146) of NRAS and KRAS was performed using the TheraScreen® NRAS Pyro kit (Qiagen).

We whould like to thank the staff of the "BioBanco del Hospital Universitario Virgen de las Nieves (Granada)" for all their support in carrying out some of the techniques studied.

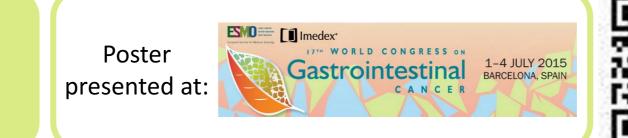
Results: From June 2013 to February 2015, 314 patients were analyzed. Of these, 134 patients (43%) had mutations in exon 2 (codons 12/13) of KRAS. 16 patients (5%) had an invalid result. From the 164 (52%) patients with wild type KRAS exon 2, 132 patients (80%) were able to analyze other RAS mutations.

A total of 12 patients (7.3%) with nonmutated KRAS exon 2 had other RAS mutations: 6 patients in the KRAS exon 3 (codon 61), 1 patient NRAS exon 2 (codon 12/13), 4 patients NRAS exon 3 (codon 61) and 1 patient in NRAS exon 4 (codon 117/146).

Conclusion: RAS mutations, in addition to KRAS exon 2 mutations, predict a lack of response to anti-EGFR therapy in patients with metastatic colorectal cancer. Approximately 20% of KRAS exon 2 wild-type tumors harbored one of the new RAS mutations, as reported in various retrospective studies.

In our series other RAS mutations were detected in 7,3%, lower than published so far.









¹Medical Oncology, Hospital Universitario San Cecilio, Granada.

²Anatomic Pathology. Hospital Universitario Virgen de las Nieves, Granada.

³Medical Oncology. Hospital Universitario Virgen de las Nieves, Granada.