gastrointestinal tumours, non-colorectal

**MOLECULAR MARKER ANALYSES OF EGFR AND KRAS FROM THE RANDOMIZED PHASE II STUDY OF NIMOTUZUMAB IN LOCALLY ADVANCED ESOPHAGEAL CANCER (NICE TRIAL)**


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**Aim:** NICE trial showed that combination of chemoradiation and nimotuzumab, a humanized antibody against EGFR, is safe and appears to increase the combined complete response (cCR) rate, defined as endoscopic and/or pathologic CR, in pts with locally advanced esophageal cancer (ASCO 2014). Here we present the results of the exploratory analyses of molecular markers and their correlation to clinical outcomes.

**Methods:** Tumor samples were obtained before chemoradiation with or without nimotuzumab. All samples were formalin-fixed and paraffin-embedded. Tumor areas were selected and macrodissected, followed by whole DNA extraction and amplification by PCR. Mutations and single nucleotide polymorphisms (SNPs) were searched in codons 12 and 13 of exon 2 for KRAS, and exons 18 to 24 for EGFR through DNA sequencing by Sanger’s methodology. Fisher’s exact test was used to compare groups.

**Results:** Molecular analyses were performed in tumor samples from 51 of the 107 randomized patients, 18 from the control arm (chemoradiation) and 37 from the experimental arm (chemoradiation plus nimotuzumab). No mutations or SNPs were identified in KRAS among the 48 samples analyzed. Indeed, no mutations were found in EGFR, but some SNPs were identified. Except for exon 21, for all other sequenced exons at least one patient had one SNP identified, more frequently in exons 20 and 23. SNPs identified in exon 20 included 167339G > A (rs10251977) and 167339G > A (rs1050171). The latter was the most frequent detected SNP and it was identified in 11 patients (3 in the control group and 8 in the nimotuzumab group). Within each treatment arm, the cCR rates were similar between patients whose tumors harboring or not the SNP rs1050171. Although not statistically significant (P = 0.074), in the nimotuzumab group, cCR rate of tumors harboring rs1050171 was nominally higher than the rate observed for tumors without this SNP (87.5% [7/8] vs. 42.9% [6/14]).

**Conclusions:** No mutations were found in KRAS or EGFR. Several EGFR SNPs were identified, being rs1050171 in exon 20 the most frequently found. Although exploratory, these results suggest an association between response to nimotuzumab and tumor biologic characteristics. Further exploration of this hypothesis is planned in a phase III trial.

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