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LONG-SURVIVORS WITH LUNG METASTASES AND KRAS MUTATIONS HAVE AN INCREASED RISK TO DEVELOP BRAIN METASTASES FROM COLORECTAL CANCER

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Background: Brain metastases (BM) occur in 1-4% of metastatic colorectal cancer (mCRC) patients (pts). Retrospective series evidence that pts with a long survival from the diagnosis of mCRC are more frequently affected. Moreover, BM seem to be associated with lung metastases and KRAS activating mutations. The identification of clinical and molecular features correlated with BM may allow the definition of a subgroup more likely to develop BM, thus to benefit from neuroimaging follow up and early treatment.

Methods: We prospectively tested the hypothesis that a higher incidence of BM occurs in a population of mCRC pts with a survival time from the diagnosis of mCRC ≥10 months, lung metastases and KRAS exons 2 and 3 mutations. Given a reported incidence of BM in unselected mCRC of around 3% (H0) and expecting an incidence in an "at risk" population selected on the basis of the 3 above reported features of 10% (H1), setting α and β errors to 0.05 and 0.10 respectively, we adopted the Fleming single-stage design for calculating the sample size of our analysis. The null hypothesis would have been rejected if at least 7 out of 104 "at risk" pts had developed BM.

Results: 623 pts, enrolled in clinical trials treated with first-line chemotherapy and bevacizumab, were included in the overall study population in order to identify 105 (16.9%) pts who simultaneously had a survival time from the diagnosis of mCRC ≥10 months, lung metastases and KRAS exons 2 and 3 mutations. 26 (4.2%) out of 623 pts developed BM. 14 out of 518 (2.7%) not "at risk" pts presented BM, while 12 out of 105 (11.4%) "at risk" pts did. The incidence of BM in the two groups differed significantly (Fisher's exact test, p = 0.0004). The null hypothesis was rejected according to the original design.

Conclusion: This analysis confirms the hypothesis that the concomitant presence of the 3 analyzed risk factors increases the probability of developing BM in mCRC patients. Based on these data, the opportunity to consider a neuroimaging exam, such as brain CT scan or MRI, in this specific population might be taken into account in order to provide an early diagnosis of BM and therefore the most appropriate therapy in an asymptomatic phase.