4- ERCC1, K-RAS and B-RAF as Novel Prognostic Markers in Colorectal Cancer

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By

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ERCC1 is a predictive marker for patient response to Oxaliplatin based chemotherapeutic regimen, the poor prognostic significance of KRAS is dispute, BRAF is a poor prognostic markers in colorectal cancer, KRAS & BRAF are predictive markers for therapeutic options and response to treatment in colorectal cancer

In this study IHC staining was done for ERCC1, KRAS &BRAF on 3-4 um section of formalin-fixed paraffin- embedded tissues of colorectal carcinomas (adenocarcinoma, mucoid adenocarcinoma & signet cell carcinoma) for 181 colorectal (stage I-IV) patients collected from oncology & gastroenterology center ,Mansoura university in the period from January 2006 to December 2014. DFS & OS are the endpoint

In this study nineteen patients (10. 5%) were stage I, fourty six patients (45. 2%) were stage II, eighty six patients (40. 5%) were stage III&thirty patients (16. 6%) were stage IV.One hundred and nine patients (60. 22%) received adjuvant therapy, sixty seven patients (37. 01%) received chemotherapy for metastatic disease.Fifty six patients had been died (30. 9%)&one hundred and twenty five had been censored (69. 1%).

regarding the relation between ERCC1 and clinicopathologic tumour features ERCC1 has no relation to tumour characteristic except tumour grade in which the tumour is more low grade in ERCC1 negative cases (58. 7%) than in ERCC1 positive cases, The DFS showed no difference between ERCC1 negative and positive cases, The median PFS for patients receiving oxaliplatin-bases chemotherapy in the metastatic setting is higher in ERCC1 negative cases (median 11 months, 95% confidence interval 7-14 months) than ERCC1 positive cases & The OS showed no difference between ERCC1 negative and positive cases.

There is no statistical significant relation between KRAS score and clinicopathologic features of the patients.The DFS showed no difference between KRAS negative and positive cases&the median OS is significantly prolonged in KRAS negative cases.

There is no statistical significant relation between BRAF score and clinicopathologic features of the patients except age in which the patients are more old age in BRAF +ve cases. The 3 and 5 years DFS is higher in BRAF negative cases However, the difference is not statistically significant &the median OS is significantly longer in BRAF negative vs. positive cases .

Conclusion

- There is statistically significant relation between ERCC1 score and tumour grade &between BRAF and patients age.
- ERCC1 score are predictive factor for response to oxaliplatin and PFS in metastatic diseases.
- BRAF score, TNM stage & histological grade are independent prognostic factors of disease free survival, but neither ERCC1 score nor KRAS score (p=0. 083) are statistically significant prognostic of DFS (p= 0. 04).
- KRAS&BRAF are prognostic factors for over all survival but ERCC1 is not statistically significant prognostic factor for over all survival in colorectal cancer, in 181 Egyptian patients with TNM staged I- IV colorectal carcinomas using IHC on formalin –fixed paraffin embedded tissues.

- IHC considered as senseitive and specific method for BRAF but only sensitive but non specific method for k ras