

FACTORS AFFECTING TUMOR RESPONSE IN METASTATIC COLORECTAL CANCER PATIENTS TO FIRST AND SECOND LINE TREATMENT

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INTRODUCTION

Metastatic colorectal cancer is the 3rdmost prevalent cancer globally and ranks 2nd in terms of cancer-related deaths. In Egypt, colon and rectal cancers were the 9th and 18thmost common malignancies and the 11th and 16th most prevalent cause of cancer-related mortality in the country, respectively. In the management of mCRC, there is need to determine predictive and prognostic factors that are likely to impact the tumor response and survival outcomes of systemic treatment. This is particularly true as the 1st and 2nd systemic lines of treatment are still the most effective treatment modalities available to control the illness. Real-world studies show that patients derive maximal benefit from 1st and 2nd line therapies as a later line of treatment do not provide a similar level of benefits. They must thus be optimized.

AIM OF THE WORK

The aim of this study was to identify the factors affecting tumor response in metastatic colorectal cancer patients to first line and second line treatment.

PATIENTS AND METHODS

A retrospective cohort study investigating the factors affecting tumor response in mCRC patients to 1st and 2nd line treatment with a sample size of 110 patients managed for mCRC between January 2019 and December 2023. The study extracted information on demographic data, clinical, pathological, laboratory data, and molecular characteristics. The results were statistically analyzed with clinical outcomes.

RESULTS

Table: Clinical Benefits: Good Response (CR or PR or SD) & Progressive Disease (Poor)

| FIRST-LINE | | | | SECOND-LINE | | | |
|---|---|----------|-----------|---|---|----------|-----------|
| Factors | 1 st Line Tumor Response Category (Good or Poor) | | | Factors | 2 nd Line Tumor Response Category (Good or Poor) | | |
| | p value | Log. Reg | ODD Ratio | | p value | Log. Reg | ODD Ratio |
| Age category (<65 or ≥65 years) | 1.000 | 0.873 | 1.085 | Age category | 0.735 | 0.640 | 1.374 |
| Sex (Male or Female) | 0.660 | 0.597 | 1.259 | Sex | 1.000 | 0.902 | 0.972 |
| Weight Status | 0.581 | 0.905 | - | Weight Status | 0.881 | 0.885 | - |
| 1 st line ECOG status during initiation of ChT | 0.849 | 0.645 | - | 2 nd line ECOG status during initiation of ChT | 0.311 | 0.222 | - |
| Diabetes | 0.114 | 0.090 | 1.364 | Diabetes | 0.130 | 0.092 | 0.324 |
| Family History of cancer | 0.529 | 0.462 | - | Family History of cancer | 0.388 | 0.336 | 0.561 |
| Tumor Variant | 0.004* | 0.026 | - | Tumor Variant | 0.313 | 0.963 | - |
| Grade (WHO system) | 0.007* | 0.005 | 0.436 | Grade (WHO system) | 0.050* | 0.061 | - |
| Obstruction | 1.000 | 0.848 | 0.922 | Obstruction | 0.769 | 0.556 | 1.417 |
| Perforation | 0.001* | 0.001 | 5.246 | Perforation | 1.000 | 0.923 | 1.080 |
| Ulceration | 0.671 | 0.555 | 0.922 | | | | |
| Tumor Deposits | 0.090 | 0.069 | 2.172 | Tumor Deposits | 1.000 | 0.880 | 1.100 |
| Margin status (+ve/ -ve) | 0.036* | 0.027 | 0.233 | Margin status | 1.000 | 0.675 | 1.667 |
| EMVI (Positive or Negative) | 0.061 | 0.058 | 0.432 | EMVI | 1.000 | 0.832 | 1.133 |
| LVI | 0.318 | 0.208 | 0.358 | LVI | 0.313 | 0.208 | 3.500 |
| Perineural Invasion | 0.232 | 0.177 | 0.517 | | | | |
| T stage | 0.661 | 0.435 | - | T stage | 0.567 | 0.242 | - |
| N stage | 0.011* | 0.006 | - | N stage | 0.316 | 0.137 | - |
| LN+ if surgery done | 0.001* | 0.001 | 10.947 | LN+ if surgery done | 0.047* | 0.043 | 10.000 |
| If Surgery done: LN ≥12 | 0.546 | 0.377 | 1.750 | If Surgery done: LN ≥12 | 1.000 | 0.660 | 1.436 |
| Greatest Primary Size | 0.082 | 0.033 | - | Greatest Primary Size | 1.000 | 0.960 | - |
| All-RAS status (mut or wt.) | 0.034* | 0.027 | 0.311 | All-RAS status | 0.152 | 0.089 | 4.333 |
| BRAF status (mut or wt.) | 0.003* | 0.009 | 0.050 | BRAF status | 1.000 | 1.000 | 1.882 |
| Primary Tumor Location (colon or rectum) | 0.602 | 0.454 | 0.664 | Primary Tumor Location | 1.000 | 0.923 | 1.080 |
| mCRC Tumor sidedness (right or left) | 0.076 | 0.063 | 0.445 | mCRC Tumor sidedness | 0.352 | 0.246 | 0.489 |
| Disease status at Diagnosis (de novo or recurrent) | 0.114 | 0.059 | 0.321 | Disease status at Diagnosis | 1.000 | 0.854 | 0.867 |
| Number of Metastatic sites | 0.152 | 0.057 | - | No. of Metastatic sites | 0.254 | 0.219 | - |
| Oligometastatic / polymetastatic | 0.058 | 0.044 | 2.428 | | | | |
| AJCC Metastatic Stage | 0.339 | 0.152 | - | AJCC Metastatic Stage | 0.144 | 0.167 | - |
| Primary Site Surgery | 0.834 | 0.291 | 0.894 | Primary Site Surgery | 1.000 | 0.923 | 0.943 |
| Metastectomy | 0.144 | 0.131 | 0.305 | PFS of first-line (≤6 m or >6m) | 0.180 | 0.126 | 0.363 |
| Chemotherapy before 1st Line | 0.175 | 0.137 | 0.371 | ChT before 1st Line | 0.694 | 0.484 | 0.542 |
| 1 st Line targeted therapy | 0.142 | 0.194 | - | 2 nd line targeted therapy | 0.757 | 0.709 | - |
| 1 st Line ChT regimen used | 0.138 | 0.266 | - | 2 nd line ChT Regimen used | 1.000 | 0.983 | - |
| 1. treatment Initiation delay (m) | 0.338 | 0.863 | - | 2. treatment Initiation delay (m) | 0.249 | 0.220 | 2.083 |
| 1. ChT Changed | 0.662 | 0.442 | 0.669 | 2. ChT Changed | 0.724 | 0.497 | 0.600 |
| 1. Dose adjustments | 0.671 | 0.555 | 0.776 | 2. Dose adjustments | 0.376 | 0.353 | 1.760 |
| 1. Maintenance | 0.012* | 0.034 | 0.108 | 2. Maintenance | 0.295 | 0.251 | 0.375 |
| 1. ChT cycles Delays * | 0.042* | 0.032 | 0.391 | 2. ChT cycles Delays * | 0.060 | 0.045 | 0.280 |
| First Line patient compliance | 0.006* | 0.004 | 3.889 | Second line patient compliance | 0.694 | 0.484 | 0.542 |
| 1 st Line pretreatment NLR | 0.087 | 0.055 | 2.440 | 2. pretreatment NLR | 0.226 | 0.206 | 2.872 |
| 1 st Line midcycle NLR | 1.000 | 0.716 | 0.774 | 2. midcycle NLR | 1.000 | 0.809 | 1.167 |
| 1 st Line pretreatment PLR | 0.402 | 0.357 | 1.477 | 2. pretreatment PLR | 0.520 | 0.202 | 0.390 |
| 1 st Line midcycle PLR | 0.303 | 0.256 | 1.753 | 2. midcycle PLR | 0.343 | 0.212 | 0.429 |
| 1 st Line pretreatment LMR | 0.477 | 0.292 | 2.500 | 2. pretreatment LMR | 1.000 | 0.578 | 2.000 |
| 1 st Line midcycle LMR | 1.000 | 0.881 | 0.889 | 2. midcycle LMR | 1.000 | 1.000 | 1.000 |
| 1 st Line pretreatment CEA | 0.163 | 0.107 | 2.759 | 2 nd line pre-tx CEA | 0.262 | 0.225 | 0.262 |
| 1 st Line pretreatment CA 19-9 | 0.297 | 0.228 | 1.901 | 2 nd line pre-tx CA 19-9 | 0.014* | 0.022 | 14.667 |
| Depicted model of tumor response | 0.001* | 0.001 | - | Depicted model | 0.001* | 0.001 | - |

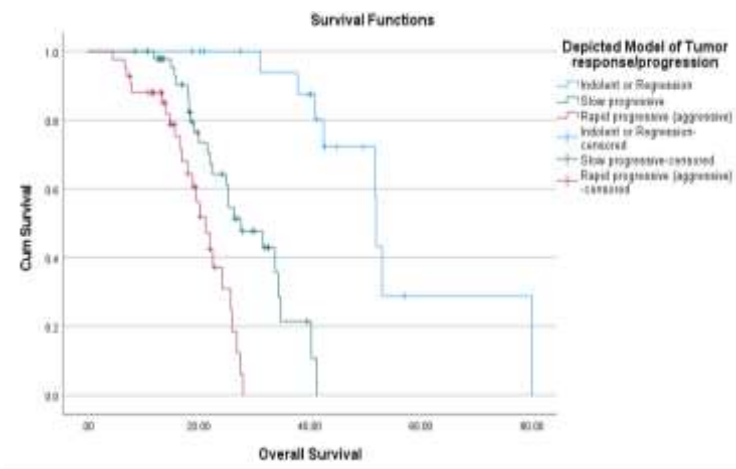


Figure 1: K-M curve for OS based on depicted model of tumor response

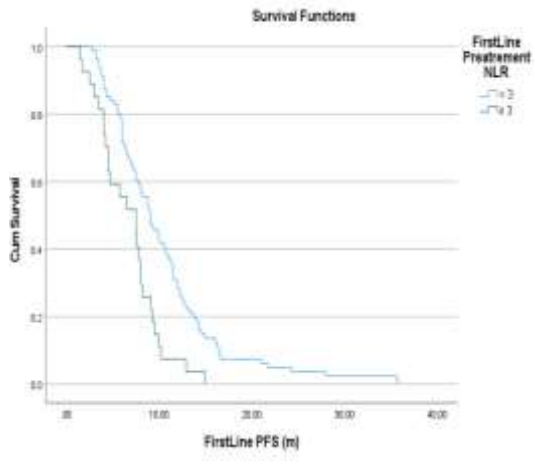


Figure 2: K-M curve for 1st line PFS based on NRL

CONCLUSION

Bowel perforation & obstruction, the histologic variant and the histologic grade of mCRC are significantly associated with survival and tumor response. In addition, LVI, PNI, or vascular invasion are significantly associated with 1stlinePFS. Classifying a malignancy as either Oligometastatic or polymetastatic has a prognostic role when the limited opportunity to remove resectable lesions is taken advantage. Surgical removal of primary tumor is significantly associated with survival outcomes. RAS mutation is significantly correlated with survival outcomes. The choice of systemic therapy and Maintenance treatment has no impact on the tumor response or survival. Chemotherapy dose adjustments (reductions) and delays negatively impact survival outcomes. CEA & CA 19.9 and LMR, PLR, & NLR have a strong correlation with survival outcomes.