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Onco News

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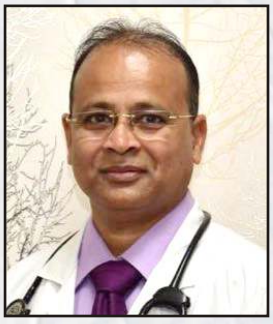
From the Desk of Editor



Dear readers,

Colorectal cancer is among those cancers whose incidence and prevalence is increasingly in India. Most disturbing aspect is that younger population is being affected and that too in most cases as advance disease. High fibre diet, reducing junk diet and meats in diet and regular exercise helps in reducing its occurrence. Regular screening programs and early detection of disease are key success for effective control and better outcome. Targeted therapies and immuno oncology drugs have added further refinements in certain subsets of metastatic disease.

Your feedback and suggestions are always welcome!

With regards
Dr. Naresh Somani
M.D., D.M.
Senior Medical Oncologist

Colorectal Cancer

Introduc1tion

Epidemiology :

- Colorectal cancer is the third most common cancer.
- It affects men and women equally.

Risk Factors :

- Average risk patients have a lifetime incidence of 5%.
- 90% of cases occur after age 50.
- 1/3 of cases are associated with familial clustering.
- Patients with familial adenomatous polyposis (FAP) have a 90% risk of colorectal cancer by age 50.
- Patients with hereditary nonpolylposisl colorectal cancer (HNPCC) have an 80% lifetime risk of developing colorectal cancer.
- Diets high in fat and low in fruits and vegetables, decreased physical activity and obesity have been associated with an increased risk.

Survival :

- 5- year overall survival rate is approximately 60%.
- 5-year survival rate for localized disease is 90%.
- 5-year survival rate for metastatic disease is 10%.

Surgery for colorectal cancer

Surgery is the mainstay of curative therapy for colorectal cancer. Curative resection requires the excision of the primary tumor and its lymphatic drainage with a margin of normal tissue.

Preoperative workup

- Precise site and local extent of the tumor should be known before laparotomy.
- Full colonoscopy (in the absence of obstruction or perforation) should be performed prior to laparotomy.
- CT of the chest, abdomen, and pelvis should be obtained to assess for distant disease.
- Preoperative CBC, chemistry profiles, and carcinoembryonic antigen (CEA) level should be obtained.

Colorectal cancer TNM staging system	
T-primary tumor	
T_{IS}	Carcinoma in situ
T1	Tumor invades submucosa
T2	Tumor invades Muscularis Propria
T3	Tumor invades through muscularis into subserosa or into nonperitonealized pericolic or perirectal tissue.
T4	Tumor invading adjacent organ(s) and/or perforates visceral peritoneum
N- Regional lymph nodes	
N0	No regional lymph node metastasis
N1	Metastasis in 1-3 regional nodes
N2	Metastasis in ≥4 regional nodes
M-Distant metastasis	
M1	Distant metastasis

Primary surgical resection

Colectomy with en bloc removal of regional lymph nodes is the procedure of choice for resectable colon cancer. At least 12 lymph nodes should be examined for accurate staging.

Minimally invasive colon cancer surgery is becoming more common but should only be performed by experienced surgeons in selected cases.

Rectal cancer

Transanal resection should only be performed for small (<3 cm), T1-T2, well to moderately differentiated, mobile tumors located within 8 cm from the anal verge, and in the absence of lymphadenopathy.

Transabdominal resection via abdonminoperineal or low anterior resection should be performed using total mesorectal excision (TME). TME reduces the incidence of positive surgical margins and resects draining lymphatics.

Resection of metastatic or recurrent disease

Resection of liver or lung metastases should generally not be considered in the setting of additional, unresectable extrahepatic or extrapulmonary disease. Solitary liver metastases have a better postresection prognosis than that of multiple liver lesions.

No definitive criteria exist (e.g. number or size of tumors) to determine eligibility for liver resection. Eligibility should instead be determined by likelihood of achieving negative margins while preserving liver functions.

Adjuvant chemotherapy for colorectal cancer

Rationale

Approximately half of patients undergoing apparently curative resection of colorectal cancer are destined to relapse and eventually die with either locally recurrent or distant metastatic disease due to the presence of residual micrometastases at the time of surgery. The aim of adjuvant chemotherapy is to eradicate these micrometastases and thereby decrease the risk of relapse.

Indications

Stage III cancers, which have spread to the nearby lymph nodes, carry a much higher risk (≃ 50%). There is substantial evidence that this risk is reduced by adjuvant chemotherapy, which is the standard of care.

Stage II cancers, which have breached the muscle layers but not spread to lymph nodes, carry an intermediate risk of ≃ 30%. There is limited evidence to support the use of adjuvant chemotherapy in these patients. However, the use of adjuvant chemotherapy should be discussed in high-risk stage II patients (T4 tumor stage, bowel perforation, or clinical obstruction).

Rectal cancer presents some special considerations. Radiotherapy targeted to the pelvis either before or after surgery, reduces local recurrence rates. Adjuvant therapy for rectal cancer may therefore include both radiotherapy and chemotherapy.

Chemotherapy used in the adjuvant setting

5-fluorouracil (5-FU) given in combination with folinic acid and Oxaliplatin (FOLFOX or Capecitabine with Oxaliplatin (CAPOX) is standard adjuvant chemotherapy.single-agent capecitabine is equivalent to 5-FU-leucovarin for adjuvant treatment of resected stage III patients, but it should be reserved for those unable to tolerate FOLFOX.

The treatment course for rectal cancer is dependent on stage:

- T1-2, N0: Resection followed by observation
- T3, N0 or T any, N1-2: Preoperative chemoradiotherapy, followed by surgery, followed by adjuvant chemotherapy (FOLFOX) for 4 months
- T4, or initially unresectable: Preoperative chemoradiotherapy, followed by resection, if possible, followed by FOLFOX for 4 months.
- Patients who do not receive preoperative chemoradiotherapy may receive it postoperatively, followed by additional adjuvant chemotherapy.

Palliative therapy for metastatic colorectal cancer

The goals of therapy are palliation and prolongation of survival. With current therapy, median survival is increased to approximately 2 to 3 years.

In most cases chemotherapy is the primary modality used, but this does not preclude the use of combined modalities such as surgery, localized radiotherapy, or ablative techniques for liver metastasis.

A small proportion of patients have oligometastatic disease, that is potentially resectable or could be made so by volume reduction using chemotherapy (down-staging).

First line chemotherapy in metastatic disease

- 5-FU/leucovorin alone or capecitabine alone is usually reserved for patients unable to tolerate combination therapy.
- Combination therapy includes a fluoropyrimidine with either oxaliplatin or irinotecan.
- Chemotherapy can be combined with targeted therapy against VEGF (Bevacizumab) or EGFR (cetuximab or panitumumab).
  EGFR targeted therapy should not be used for RAS mutant tumors.or left sided tumors.
- Capecitabine, an orally administered prodrug of 5-FU, is an effective part of combination therapy in the metastatic setting.
- Bevacizumab an antivascular endothelial growth factor (VEGF) monoclonal antibody, has been shown to improve survival in the metastatic setting.
- Cetuximab, a chimeric antiepidermal growth factor receptor (EGFR) monoclonal antibody, and panitumumab, a human anti-EGFR monoclonal antibody, have both been shown to improve outcomes in the first line metastatic setting in combination with chemotherapy for patients with RAS wild-type tumors.

In Lighter vain - Beware of reading health books ! You may die of misprint !!

Contd.

BevaciRel™

Bevacizumab injection (100 mg/4 ml and 400 mg/16 ml) for I.V. use

Reliance Life Sciences

World's first bevacizumab biosimilar

Extensive characterization studies

- Orthogonal biochemical and structural characterization

Strong clinical biosimilarity with comparativ clinical outcomes

- ORR[1] at 25 weeks: BevaciRel™ (59.46%) vs. Reference biologic (66.67%)
- PFS[2] at 25 weeks: BevaciRel™ (3.47 months) vs. Reference biologic (3.39 months)
- Comparable pharmacokinetic and safety profile

Manufactured in fully-integrated facility

- Cloning to commercial product development in India's largest monoclonal antibody facility

In metastatic colorectal cancer[3]

Addition of bevacizumab results in statistically significant and clinically meaningful improvement in survival among patients with mCRC

- The median survival was 20.3 months vs.15.6 months in IFL plus bevacizumab as compared with IFL plus placebo, corresponding to a HR 0.66 (P<0.001)

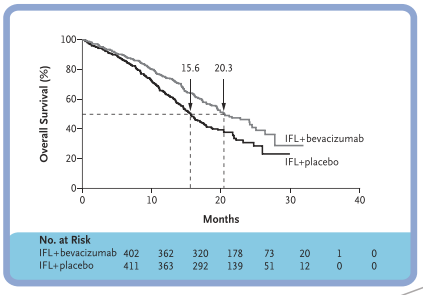


Figure 1. Kaplan-Meier Estimates of Survival. - The median duration of survival (Indicated by the dotted lines was 20.3 months in the group given Irinotecan, Flourouracil and Leucovorin (IFL) plus bevacizumab, as compared with 15.6 months in the group given IFL plus placebo, corresponding to a hazard ratio for death of 0.66 (P<0.001)

Second line chemotherapy

Patients who progressed on first-line therapy with oxaliplatin and bevacizumab should be treated with irinotecan with or without 5-FU, and with or without bevacizumab, cetuximab or panitumumab (if RAS wild-type). In RAS wild-type tumors, cetuximab and panitumumab have both shown efficacy as single agents and in combination.

Potential second line regimens (assuming first line treatment with oxaliplatin) include FOLFIRI-bevacizumab, FOLFIRI-cetuximab or panitumumab, FOLFIRI-aflibercept, irinotecan-cetuximab or panitumumab, single-agent irinotecan, or single-agent cetuximab or panitumumab.

Subsequent chemotherapy

With increasing survival, colorectal cancer patients are exposed to multiple lines of therapy.

Recent data provide support for the use of regorafenib, a multityrosine kinase inhibitor in metstatic colon cancer patients.

Role of Immuno oncology drugs

Based on tumor expression of MSI-H, patient can be treated with PD-1/PD-L1 inhibitor drugs like Pemborolizumab or Nivolomab.

Ongoing Clinical Trials

- **Project # MYL-1402O-3001:**
  Multicentre, Double-Blind, Randomized, Parallel-Group Study to Assess the Efficacy and Safety of MYL-1402O Compared With Avastin®, in the First -line treatment of Patient with Stage IV Non-Squamous Non-Small Cell Lung Cancer.
- **CLDK378A2301:**
  A phase III multicenter, randomized study of oral LDK378 versus standard chemotherapy in previously untreated adult patients with ALK rearranged (ALK-positive), stage IIIB or IV, non-squamous non-small cell lung cancer (Phase-III).
- **Protocol No: CLDK378AIN01:**
  A real-world, open-label, multi-center, prospective, non-interventional (observational) study to evaluate the effectiveness and tolerability of ceritinib in Indian pativvents with ALK positive metastatic non-small cell lung cancer who have progressed or are intolerant to crizotinib.
- **Protocol No. WOC/AMS/CT-44/14:**
  A Surveillance Study on the Antibiotic susceptibility pattern of bacterial isolates collected from patients at various Indian Tertiary Care Hospitals (ASPIRE INDIA)
- **Protocol Title: CPZP034AIC04 Parachute:**
  Pazopanib Real-world Assessment of Clinical effectiveness and safety in patients who have Undergone treatment in different settings in advanced renal cell carcinoma; a prospective, non-interventional, observation study.

Onco-Facts

1. Abiraterone acetate with caastration has shown marked improvemnent in survival comared with castration in treatment naive metastatic prostate cancer ;and can be cosidered as standard of care in this setting.
2. Immuno oncology drugs like Nivolumab and Atezolizumab has shown better results compare to available treatment options in second line treatment of lung, kidney cancers and head and neck cancers.
3. CDK4/6 inhibitor drugs like Ribociclib and Palbociclib in combination with hormonal treatment like Letrozole or Fulvistrant has almost doubled the progression free survival in metastatic breast cancer.

Recent Activities of Somex Research & Health Pvt. Ltd.

- CME and International speaker program on Management of metastatic Breast cancer on 17 th March 2018
- CME on “Immuno-oncology: Spreading Its Wings” on 4th March 2018.
- Organized launch meeting and CME of New products of multi national giant, Novartis in Breast Cancer on 23rd Feb 2018
- CME on "ROS-1 Positive Lung Cancer" on 31st January 2018
- Conducted Indian Breast Cancer Conference, October 2017

BOOK - POST

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If undelivered please return to:

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