

# Diagnosis and Treatment of Colorectal Cancer: A Review

Ashlesha Deverakonda\*

Department of Pharmaceutical Analysis and Quality Assurance, Malla Reddy College of Pharmacy,  
Hyderabad, India

## Review Article

Received: 02/08/2016  
Revised: 04/08/2016  
Accepted: 10/08/2016

### \*For Correspondence

Ashlesha Devarakonda,  
Department of Pharmaceutical  
Analysis and Quality Assurance,  
Malla Reddy College of  
Pharmacy, Hyderabad, India

### E-mail:

[Ashlesha.sweet4@gmail.com](mailto:Ashlesha.sweet4@gmail.com)

**Keywords:** Colorectal cancer,  
Tumour, Sigmoidoscopy,  
Chemotherapy

## ABSTRACT

Colorectal cancer is a type of a cancer which infects the parts of digestive system. There are many ways of treatments for this type of cancer which cannot give the complete prevention of colon cancer. The prevention is based on many factors described below and types of therapies choosey are based on the stage and type of the colon cancer. The complete prevention is done when the patient follows all the medication regularly and when the preventive measures followed strictly. Now days the mostly effected and causing cancer is colorectal cancer.

## INTRODUCTION

Colorectal tumour (otherwise called colon malignancy, rectal disease, or gut growth) is the advancement of growth from the colon or rectum (parts of the digestive organ). It is because of the anomalous development of cells that can attack or spread to different parts of the body. Signs and side effects may incorporate blood in the stool, an adjustment in defecations, weight reduction, and feeling tired constantly. Most colorectal diseases are because of maturity and way of life variables with just a little number of cases because of hidden hereditary issue. Some danger elements incorporate eating regimen, corpulence, smoking, and absence of physical action. Dietary elements that build the danger incorporate red and handled meat and in addition liquor. Another danger element is provocative inside ailment, which incorporates Crohn's illness and ulcerative colitis [1-4]. Portions of the acquired hereditary issue that can bring about colorectal disease incorporate familial adenomatous polyposis and innate non-polyposis colon malignancy; in any case, these speak to under 5% of cases. It normally begins as an amiable tumor, frequently as a polyp, which after some time gets to be harmful. Inside disease might be analyzed by acquiring an example of the colon amid a sigmoidoscopy or colonoscopy. This is then trailed by medicinal imaging to figure out whether the illness has spread. Screening is compelling for keeping and diminishing passings from colorectal growth. Screening is suggested beginning from the age of 50 to 75. Aspirin and other non-steroidal mitigating drugs diminish the danger. Their general use is not suggested for this reason, be that as it may, because of reactions [4-8].

## DIAGNOSIS OF COLORECTAL CANCER

### Faecal Occult Blood Test (FOBT)

Medications utilized for colorectal tumor may incorporate some blend of surgery, radiation treatment, chemotherapy and focused on treatment [9]. Tumors that are kept to the mass of the colon might be treatable with surgery while growth that has spread broadly are normally not reparable, with administration concentrating on enhancing personal satisfaction and side effects. Five year survival rates in the United States are around 65%. This,

be that as it may, relies on upon how exceptional the tumor is, regardless of whether all the disease can be expelled with surgery, and the individual's general wellbeing. All around, colorectal malignancy is the third most normal sort of growth making up around 10% of all cases. In 2012, there were 1.4 million new cases and 694,000 passings from the infection. It is more regular in created nations, where more than 65% of cases are found. It is less basic in ladies than men [10-12].

### **Stool DNA Testing**

Stool DNA [sDNA] testing depends on the idea that there is ceaseless and bottomless shedding of dysplastic cells into the lumen as the stool goes through the colon [13].

### **Stool Nucleic Acids**

In prior blinded screening concentrates, just about portion of the screenrelevant neoplasms were recognized by sDNA testing. The execution was traded off by different specialized constraints [14,15].

### **Multitarget Stool DNA Test**

Considers have demonstrated that blends of atomic markers in stool DNA testing produce high identification rates for both colorectal disease and propelled adenomas [16,17].

### **Epigenetic Biomarkers: DNA Methylation, Hypermethylation, And Hypomethylation Markers**

Colorectal tumor is driven by the collection of hereditary variations from the norm and epigenetic modifications. Epigenetic adjustments, especially unusual DNA methylation [including hypomethylation and hypermethylation] are presently thought to be one of the most punctual anomalies in the movement of adenoma to carcinoma.

### **Genetic Biomarkers**

The most widely recognized hereditary biomarkers explored to analyze colorectal malignancy incorporate Adenomatous polyposis coli (APC), P53, KRAS, and BAT 26. APC and P53 are essential tumor silencer qualities transformed in CRC . KRAS and BRAF are oncogenes changed in CRC [18-22].

### **Long DNA**

Long DNA is gotten from dangerous or precancerous cells shed from dysplastic mucosa which have not experienced apoptosis. The last is the physiological instrument that kills most typical colonic epithelial cells and results in DNA being divided into little sizes.

### **And Many Other Tests for Diagnosis They Are**

Fecal protein examine biomarkers, Microsatellite Instability, Serological biomarkers, Urine Biomarkers, Cancer identification Vs. Polyp discovery, Adherence and patient elements [23-25].

## **PREVENTION OF COLORECTAL CANCER**

It has been assessed that about portion of colorectal disease cases are because of way of life variables and around a fourth of all cases are preventable [26]. Expanding reconnaissance, taking part in physical movement, devouring an eating routine high in fiber, and diminishing smoking and liquor utilization diminish the danger [27,28].

### Lifestyle

Current dietary proposals to avoid colorectal growth incorporate expanding the utilization of entire grains, leafy foods, and diminishing the admission of red meat and prepared meats. Higher physical action is likewise prescribed. Physical activity is connected with an unobtrusive decrease in colon yet not rectal tumor hazard. Sitting routinely for delayed periods is connected with higher mortality from colon tumor. The danger is not nullified by customary activity, however it is brought down. The proof for fiber and leafy foods however is poor.

### Medication

Aspirin and celecoxib seem to diminish the danger of colorectal disease in those at high hazard. Headache medicine is prescribed in the individuals who are 50 to 60 years of age, don't have an expanded danger of dying, and are at danger for cardiovascular infection to forestall colorectal growth [29]. It is not prescribed in those at normal danger. There is speculative confirmation for calcium supplementation yet it is not adequate to make a proposal. Vitamin D admission and blood levels are connected with a lower danger of colon disease.

### Screening

As more than 80% of colorectal tumors emerge from adenomatous polyps, screening for this malignancy is successful for early discovery as well as for avoidance. Finding of instances of colorectal growth through screening has a tendency to happen 2–3 years before conclusion of cases with side effects. Any polyps that are identified can be expelled, for the most part by colonoscopy or sigmoidoscopy, and consequently kept from turning carcinogenic. Screening can possibly diminish colorectal malignancy passings by 60%.

The four fundamental screening tests are fecal mysterious blood testing, adaptable sigmoidoscopy, colonoscopy, and stool DNA screening test. Of the three, no one but sigmoidoscopy can't screen the right half of the colon where 42% of malignancies are found [30]. Virtual colonoscopy through a CT examine shows up on a part with standard colonoscopy for identifying malignancies and expansive adenomas yet is costly, connected with radiation presentation, and can't evacuate any distinguished unusual developments like standard colonoscopy scan [31].

Fecal mysterious blood testing (FOBT) of the stool is ordinarily suggested at regular intervals and can be either guaiac based or immunochemical. In the event that strange FOBT results are discovered, members are commonly eluded for a subsequent colonoscopy examination. FOBT screening decrease colorectal malignancy mortality by 16% and among those taking an interest in screening colorectal disease mortality can be lessened up to 23%, in spite of the fact that it has not been demonstrated to diminish all-cause mortality. Immunochemical tests are exceptionally precise and don't require dietary or solution changes before testing [32-34].

The multitarget stool DNA screening test is a noninvasive test used to screen for the nearness of colorectal tumor or precancerous injuries. It utilizes a feces test to recognize biomarkers connected with colorectal tumor and

precancerous injuries, including changed DNA and blood hemoglobin. A positive result may demonstrate the nearness of precancerous injuries or colorectal tumor, and thought to be trailed by colonoscopy. The American Cancer Society suggests screening with multitarget sDNA testing like clockwork, beginning at age 50 [35,36].

## TREATMENT OF COLORECTAL CANCER

### Treatment of Colon Cancer at Stage 0

Since stage 0 colon growths have not developed past the internal covering of the colon, surgery to take out the malignancy is normally all that is required. This should be possible much of the time by evacuating the polyp (polypectomy) or nearby extraction through a colonoscope [37]. Expelling part of the colon (fractional colectomy) may sporadically be required if a tumor is too huge to be evacuated by neighborhood extraction [38].

### Treatment of Colon Cancer at Stage 1

Stage I colon diseases have developed into the layers of the colon divider, yet they have not spread outside the colon divider itself (or into the adjacent lymph hubs).

Stage I incorporates diseases that were a piece of a polyp. In the event that the polyp is expelled totally amid colonoscopy, with no malignancy cells at the edges of the evacuated test, no other treatment might be required [39]. On the off chance that the tumor in the polyp is high review or there are growth cells at the edges of the polyp, more surgery might be prompted. You may likewise be encouraged to have more surgery if the polyp couldn't be expelled totally or on the off chance that it must be evacuated in numerous pieces, making it difficult to check whether tumor cells were at the edges [40,41].

For diseases not in a polyp, fractional colectomy — surgery to expel the segment of colon that has malignancy and close-by lymph hubs — is the standard treatment. You normally won't require any extra treatment.

### Treatment of Colon Cancer at Stage 2

Numerous stage II colon tumors have become through the mass of the colon, and potentially into close-by tissue, however they have not yet spread to the lymph hubs [42].

Surgery to evacuate the segment of the colon containing the tumor alongside close-by lymph hubs (incomplete colectomy) might be the main treatment required. Be that as it may, your specialist may prescribe adjuvant chemotherapy if your growth has a higher danger of returning due to specific variables, for example,

The tumor looks extremely irregular (is high review) when seen under a magnifying lens.

The malignancy has developed into close-by blood or lymph vessels [43].

The specialist did not evacuate no less than 12 lymph hubs.

Disease was found in or close to the (edge) of the surgical example, implying that some malignancy may have been deserted. The disease had closed off (deterred) the colon. The disease brought about a puncturing (opening) in the mass of the colon. Not all specialists concede to when chemo thought to be utilized for stage II colon diseases. It's critical for you to talk about the upsides and downsides of chemo with your specialist, including the amount it may diminish your danger of repeat and what the reasonable symptoms will be. On the off chance that chemo is utilized, the principle choices incorporate 5-FU and leucovorin, or capecitabine, however different blends may likewise be utilized [44]. On the off chance that your specialist is not certain the greater part of the growth was expelled on the

grounds that it was developing into different tissues, he or she may encourage radiation treatment to attempt to murder any outstanding disease cells in the zone of your belly where the malignancy was developing.

### **Treatment of Colon Cancer at Stage 3**

Stage III colon growths have spread to close-by lymph hubs, yet they have not yet spread to different parts of the body.

Surgery to evacuate the area of the colon with the disease alongside close-by lymph hubs (fractional colectomy) trailed by adjuvant chemo is the standard treatment for this stage <sup>[45]</sup>.

For chemo, either the FOLFOX (5-FU, leucovorin, and oxaliplatin) or CapeOx (capecitabine and oxaliplatin) regimens are utilized frequently, however a few patients may get 5-FU with leucovorin or capecitabine alone in light of their age and wellbeing needs <sup>[46]</sup>.

Your specialists may likewise exhort radiation treatment if your specialist supposes some malignancy cells may have been deserted after surgery.

Radiation treatment and/or chemo might be possibilities for individuals who aren't sufficiently sound for surgery.

### **Treatment of Colon Cancer at Stage 4**

Stage IV colon tumors have spread from the colon to inaccessible organs and tissues. Colon disease regularly spreads to the liver, however it can likewise spread to different places, for example, the lungs, peritoneum (the coating of the stomach cavity), or too far off lymph hubs.

Much of the time surgery is unrealistic to cure these tumours. Be that as it may, if there are just a couple of little zones of growth spread (metastases) in the liver or lungs and they can be evacuated alongside the colon disease, surgery may help you live more and may even cure you. This would mean having a fractional colectomy to expel the segment of the colon containing the growth alongside close-by lymph hubs, in addition to surgery to evacuate the territories of tumor spread. Chemo is normally given too, before and/or after surgery. At times, hepatic supply route implantation might be utilized if the malignancy has spread to the liver.

On the off chance that the metastases can't be expelled in light of the fact that they are too expansive or there are excessively numerous of them, chemo might be given before any surgery (neoadjuvant chemo). At that point, if the tumors shrink, surgery to expel them might be attempted. Chemo would then be given again after surgery. For tumors in the liver, another alternative might be to crush them with removal or embolization <sup>[47]</sup>.

On the off chance that the malignancy has spread a lot to attempt to cure it with surgery, chemo is the primary treatment. Surgery may in any case be required if the malignancy is hindering the colon (or is liable to do as such). In some cases, such surgery can be stayed away from by embedding's a stent (an empty metal or plastic tube) into the colon amid a colonoscopy to keep it open. Something else, operations, for example, a colectomy or redirecting colostomy (cutting the colon over the level of the disease and connecting the end to an opening in the skin on the stomach area to permit waste out) might be utilized.

In the event that you have stage IV malignancy and your specialist prescribes surgery, it's critical to comprehend the objective of the surgery — whether it is to attempt to cure the growth or to forestall or alleviate manifestations of the illness <sup>[48]</sup>.

Most patients with stage IV malignancy will get chemo and/or focused on treatments to control the disease. Probably the most ordinarily utilized regimens include:

FOLFOX: leucovorin, 5-FU, and oxaliplatin (Eloxatin)

FOLFIRI: leucovorin, 5-FU, and irinotecan (Camptosar)

CapeOX: capecitabine (Xeloda) and oxaliplatin

FOLFOXIRI: leucovorin, 5-FU, oxaliplatin, and irinotecan

One of the above mixes in addition to either a medication that objectives VEGF (bevacizumab [Avastin], ziv-aflibercept [Zaltrap], or ramucirumab [Cyramza]), or a medication that objectives EGFR (cetuximab [Erbixim] or panitumumab [Vectibix])

5-FU and leucovorin, with or without a focused on medication

Capecitabine, with or without a focused on medication

Irinotecan, with or without a focused on medication

Cetuximab alone

Panitumumab alone

Regorafenib (Stivarga) alone

Trifluridine and tipiracil (Lonsurf)

The decision of regimens relies on upon a few variables, including any past medications you've had and your general wellbeing. In the event that one of these regimens is no more viable, another might be attempted.

For cutting edge growths, radiation treatment can likewise be utilized to avert or diminish manifestations, for example, torment. While it might shrivel tumors for a period, it is unrealistic to bring about a cure. On the off chance that your specialist suggests radiation treatment, it's vital that you comprehend the objective of treatment.

## Management

The treatment of colorectal tumor can be gone for cure or mitigation. The choice on which expect to embrace relies on upon different components, including the individual's wellbeing and inclinations, and also the phase of the tumor. At the point when colorectal malignancy is gotten early, surgery can be corrective. Be that as it may, when it is distinguished at later stages (for which metastases are available), this is more improbable and treatment is frequently coordinated at concealment, to assuage side effects brought about by the tumor and keep the individual as agreeable as would be prudent <sup>[49]</sup>.

## Surgery

On the off chance that the disease is found at an early stage, it might be expelled amid a colonoscopy. For individuals with confined disease, the favored treatment is finished surgical expulsion with sufficient edges, with the endeavor of accomplishing a cure. This should either be possible by an open laparotomy or in some cases laparoscopically. The colon may then be reconnected or a man may have a colostomy <sup>[50]</sup>.

On the off chance that there are just a couple of metastases in the liver or lungs they may likewise be evacuated. At times chemotherapy is utilized before surgery to contract the malignancy before endeavoring to expel it. The two most regular locales of repeat of colorectal growth are the liver and lungs.

## Chemotherapy

In both disease of the colon and rectum, chemotherapy might be utilized as a part of expansion to surgery in specific cases. The choice to include chemotherapy in administration of colon and rectal malignancy relies on upon the phase of the malady [51-55].

In Stage I colon disease, no chemotherapy is offered, and surgery is the conclusive treatment. The part of chemotherapy in Stage II colon malignancy is easily proven wrong, and is generally not offered unless danger components, for example, T4 tumor or deficient lymph hub testing is recognized. It is additionally realized that the patients who convey anomalies of the bungle repair qualities don't profit by chemotherapy. For stage III and Stage IV colon tumor, chemotherapy is an indispensable piece of treatment [56-60].

In the event that tumor has spread to the lymph hubs or far off organs, which is the situation with stage III and stage IV colon growth individually, including chemotherapy specialists fluorouracil, capecitabine or oxaliplatin builds future. In the event that the lymph hubs don't contain malignancy, the advantages of chemotherapy are questionable. On the off chance that the tumor is broadly metastatic or unresectable, treatment is then palliative. Normally in this setting, various diverse chemotherapy solutions might be utilized. Chemotherapy drugs for this condition may incorporate capecitabine, fluorouracil, irinotecan, oxaliplatin and UFT. The medications capecitabine and fluorouracil are exchangeable, with capecitabine being an oral solution while fluorouracil being an intravenous prescription. Some particular regimens utilized for CRC are FOLFOX, FOLFOXIRI, and FOLFIRI [61-64]. Antiangiogenic medications, for example, bevacizumab are regularly included first line treatment. Another class of medications utilized as a part of the second line setting are epidermal development component receptor inhibitors, of which the two FDA affirmed ones are cetuximab and panitumumab.

The essential contrast in the way to deal with low stage rectal tumor is the joining of radiation treatment. Frequently, it is utilized as a part of conjunction with chemotherapy in a neoadjuvant design to empower surgical resection, so that eventually as colostomy is not required. Be that as it may, it may not be conceivable in low lying tumors, in which case, a changeless colostomy might be required. Stage IV rectal tumor is dealt with like stage IV colon malignancy [64-67].

### **Radiation Therapy**

While a blend of radiation and chemotherapy might be valuable for rectal malignancy, its utilization in colon growth is not normal because of the affectability of the guts to radiation. Generally with respect to chemotherapy, radiotherapy can be utilized as a part of the neoadjuvant and adjuvant setting for a few phases of rectal tumor [68].

### **Radiation Therapy for Colorectal Cancer**

Radiation treatment utilizes high-vitality beams, (for example, x-beams) or particles to obliterate disease cells. Chemotherapy can make radiation treatment more compelling against some colon and rectal malignancies. Utilizing these 2 medications together is called chemo radiation or chemo radiotherapy [69].

At the point when is radiation treatment utilized for colorectal tumor?

### **For Colon Malignancy, Radiation Treatment Might be Utilized**

After surgery, if the disease has appended to an inside organ or the coating of the belly. In the event that this happens, the specialist can't be sure that all the tumor has been expelled. Radiation treatment might be utilized to attempt to murder any disease cells that may have been deserted.

To control diseases in individuals who are not sufficiently beneficial for surgery or to ease (whitewash) indications in individuals with cutting edge tumor bringing about intestinal blockage, dying, or torment [70-75].

To treat disease that has spread to different zones, for example, the bones or cerebrum.

### **Radiation Treatment Might be Utilized**

Either before or after surgery to keep the disease from returning. For this situation, it is frequently given alongside chemotherapy. Numerous specialists now support giving radiation treatment before surgery, as it might make it less demanding to expel the malignancy, particularly if the disease's size and/or position may make surgery troublesome [76].

To control rectal diseases in individuals who are not sufficiently beneficial for surgery or to ease (mitigate) indications in individuals with cutting edge malignancy bringing on intestinal blockage, dying, or agony.

To treat growth that has spread to different territories, for example, the bones or cerebrum.

### **Types of Radiation Therapy**

Different types of radiation therapy can be used to treat colon and rectal cancers.

#### **External-Beam Radiation Therapy**

##### ***For colon malignancy, radiation treatment might be utilized***

After surgery, if the disease has appended to an inside organ or the coating of the belly. In the event that this happens, the specialist can't be sure that all the tumor has been expelled. Radiation treatment might be utilized to attempt to murder any disease cells that may have been deserted [77-82].

To control diseases in individuals who are not sufficiently beneficial for surgery or to ease (whitewash) indications in individuals with cutting edge tumor bringing about intestinal blockage, dying, or torment.

To treat disease that has spread to different zones, for example, the bones or cerebrum.

##### ***For rectal disease, radiation treatment might be utilized***

Either before or after surgery to keep the disease from returning. For this situation, it is frequently given alongside chemotherapy. Numerous specialists now support giving radiation treatment before surgery, as it might make it less demanding to expel the malignancy, particularly if the disease's size and/or position may make surgery troublesome [83,84].

To control rectal diseases in individuals who are not sufficiently beneficial for surgery or to ease (mitigate) indications in individuals with cutting edge malignancy bringing on intestinal blockage, dying, or agony.

To treat growth that has spread to different territories, for example, the bones or cerebrum.

##### ***Internal radiation therapy (brachytherapy)***

This sort of radiation treatment can be utilized to treat some rectal malignancies. For this treatment, a radioactive source is put inside your rectum by or into the tumor. The upside of this methodology is that the radiation achieves the rectum without going through the skin and different tissues of the belly, which implies it is more averse to bring about symptoms [85-87].

***Endocavitary radiation therapy***

For this treatment, a little gadget is set through the rear-end and into the rectum to convey high-force radiation for a couple of minutes. This is ordinarily done in 4 medications (or less), with around 2 weeks between every treatment. This can let a few patients, especially elderly patients, maintain a strategic distance from significant surgery and a colostomy. This kind of treatment is utilized for some little rectal malignancies. Infrequently outer shaft radiation treatment is additionally given <sup>[88]</sup>.

***Interstitial brachytherapy***

For this treatment, a tube is put into the rectum and specifically into the growth. Little pellets of radioactive material are then put into the tube for a few minutes. The radiation ventures just a short separation, restricting the impacts on encompassing sound tissues. It is some of the time used to treat individuals with rectal malignancy, especially individuals who are not sufficiently beneficial for surgery. This should be possible a couple times each week for two or three weeks, however it can likewise be only a one-time methodology <sup>[89]</sup>.

***Ablation and embolization for colorectal cancer***

At the point when colorectal growth has spread to different organs, for example, the liver, the metastases can in some cases be evacuated by surgery or annihilated by different methods, for example, removal or embolization. This may help a man live more. Removal and embolization can regularly be great choices for individuals whose tumor can't be cured with surgery or who can't have surgery for different reasons. Commonly, you won't have to stay in the clinic for these medications <sup>[90,91]</sup>.

**Ablation**

Removal alludes to medicines that wreck tumors without evacuating them. These are regularly used to treat malignancy spread in the liver, however they can be utilized to treat tumors in different spots.

**Radiofrequency ablation:**

Radiofrequency removal (RFA) utilizes high-vitality radio waves to slaughter tumors. A slim, needle-like test is put through the skin and into the tumor utilizing CT or ultrasound direction. An electric current is then go through the tip of the test, discharging high-recurrence radio waves that warmth the tumor and wreck the growth cells <sup>[92-94]</sup>.

***Ethanol (alcohol) ablation***

In this system, otherwise called percutaneous ethanol infusion (PEI), concentrated liquor is infused straightforwardly into the tumor to execute growth cells. This is normally done through the skin utilizing a needle, which is guided by ultrasound or CT examines <sup>[95-97]</sup>.

***Cryosurgery (cryotherapy)***

Cryosurgery annihilates the tumor by solidifying it with a slight metal test. The test is guided through the skin and into the tumor utilizing ultrasound <sup>[98]</sup>. At that point extremely cool gasses are gone through the test to solidify the tumor, murdering the malignancy cells. This strategy can treat bigger tumors than the other removal methods, however it here and there requires general anesthesia (you are in a profound rest) <sup>[99]</sup>.

### Palliative Care

Palliative consideration is medicinal consideration which concentrates on treatment of indications from genuine disease, similar to tumor, and enhancing personal satisfaction. Palliative look after any individual who has propelled colon malignancy or has huge manifestations.

Contribution of palliative consideration might be advantageous to enhance the personal satisfaction for both the individual and his or her family, by enhancing indications, tension and forestalling admissions to the clinic.

In individuals with serious colorectal malignancy, palliative consideration can comprise of methods that diminish side effects or difficulties from the tumor however don't endeavor to cure the hidden growth, in this way enhancing personal satisfaction. Surgical choices may incorporate non-therapeutic surgical expulsion of a portion of the growth tissue, bypassing part of the digestion systems, or stent position. These methodology can be considered to enhance manifestations and lessen difficulties, for example, seeping from the tumor, stomach torment and intestinal deterrent. Non-agent techniques for symptomatic treatment incorporate radiation treatment to reduction tumor size and in addition torment pharmaceuticals [100].

### REFERENCES

1. Haggard FA and Boushey RP. Colorectal cancer epidemiology: Incidence, mortality, survival and risk factors. *Clin Colon Rectal Surg.* 2009;22:191-197.
2. Yu XF, et al. miR-93 suppresses proliferation and colony formation of human colon cancer stem cells. *World J Gastroenterol.* 2011;17:4711-4717.
3. Dalerba P, et al. Phenotypic characterization of human colorectal cancer stem cells. *Proc Natl Acad Sci USA.* 2007;104:10158-10163.
4. Carroll D, et al. Generalist palliative care delivered by community nurses. *J Comm Pub Health Nurs.* 2016;2:122.
5. Jerkic S, et al. Colorectal cancer in two pre-teenage siblings with familial adenomatous polyposis. *Eur J Pediatr.* 2015;164:306-310.
6. Patel SG and Ahnen DJ. Familial colon cancer syndromes: An update of a rapidly evolving field. *Curr Gastroenterol Rep.* 2012;14:428-438.
7. Boman BM and Huang E. Human colon cancer stem cells: A new paradigm in gastrointestinal oncology. *J Clin Oncol.* 2008;26:2828-2838.
8. Sammut J, et al. Cancer/testis antigens and colorectal cancer. *J Genet Syndr Gene Ther.* 2013;4:149.
9. Dabak TK, et al. Diagnosis of osteoporosis and radiotherapy induced fracture by f-18 fdg pet/ct in a case with colon cancer. *OMICS J Radiol.* 2016;5:212.
10. Palaghia M, et al. Metastatic colorectal cancer: Review of diagnosis and treatment options. *Journal of Surgery.* 2015;10:249-256.
11. Dabak TK, et al. Diagnosis of osteoporosis and radiotherapy induced fracture by f-18 fdg pet/ct in a case with colon cancer. *OMICS J Radiol.* 2016;5:212.
12. Kaur A, et al. Recognizing diagnostic gap in colorectal cancer. *Intern Med.* 2016; 6:219

13. Zhu H and Zheng S. Sequential combination of serum pyruvate kinase isoenzyme m2 and colonoscopy-a promising screening protocol for colorectal cancer early diagnosis. *J Biosens Bioelectron*. 2011;S2:002.
14. Skvortsov S, et al. Different proteome pattern of epidermal growth factor receptor-positive colorectal cancer cell lines that are responsive and nonresponsive to c225 antibody treatment. *Mol Cancer Ther*. 2004;3:1551-1558.
15. Garcia SB, et al. Neuropeptides in the development of colon cancer. *Can Surg*. 2016;1:104.
16. Montagut C, et al. Identification of a mutation in the extracellular domain of the epidermal growth factor receptor conferring cetuximab resistance in colorectal cancer. *Nat Med*. 2012;18:221-223.
17. Fanale D, et al. MicroRNAs in colorectal cancer drug resistance: shooters become targets. *J Carcinogene Mutagene*. 2013;4:136.
18. Kahouli I, et al. Characterization of *L. reuteri* ncimb 701359 probiotic features for potential use as a colorectal cancer biotherapeutic by identifying fatty acid profile and anti-proliferative action against colorectal cancer cells. *Drug Des*. 2016;5:131.
19. Yang L, et al. Associations between markers of colorectal cancer stem cells, mutations, miRNA, and clinical characteristics of ulcerative colitis. *Transl Med*. 2016;6:168.
20. Fung KYC, et al. Analysis of 32 blood-based protein biomarkers for their potential to diagnose colorectal cancer. *J Mol Biomark Diagn*. 2013;S6:003.
21. Yung-Bin K, et al. Fecal miRNAs as biomarkers for the detection of colorectal cancer. *J Gastroint Dig Syst*. 2013;S12:016.
22. Galizia G, et al. Different biomarkers address different colorectal cancer stem cell populations: who's the killer? *J Mol Biomarkers Diagn*. 2012;S8:004.
23. Mazilu L, et al. Colorectal cancer screening: is there a role for stool dna testing? *J carcinog & mutagen*. 2014;S10: 006.
24. Henry T Lynch MD, et al. What can be done to improve uptake of genetic testing for inherited colorectal cancer susceptibility? *J Gastroint Dig Syst*. 2013;3:157.
25. Allegra CJ, et al. American society of clinical oncology provisional clinical opinion: Testing for kras gene mutations in patients with metastatic colorectal carcinoma to predict response to anti-epidermal growth factor receptor monoclonal antibody therapy. *J Clin Oncol*. 2009;27:2091-2096.
26. Manzano A and P. Pérez-Segura. Chemoprevention in sporadic colorectal cancer: The role of salicylates, nsoids and coxibs. *J Cancer Sci Ther*. 2011;S3:005.
27. Colditz GA and Hank Dart SM. Massachusetts leads the nation in colorectal cancer screening: What lessons can we learn for implementing prevention - translating epidemiology to practice? *Epidemiol*. 2013;3: e111.
28. Barone M and Leo AD. Estrogen receptor beta in colorectal cancer prevention: Do we have conclusive proof? *J Genet Syndr Gene Ther*. 2013;4:201.
29. Rosa LS, et al. Anticancer properties of phenolic acids in colon cancer – a review. *J Nutr Food Sci*. 2016;6:468.
30. Pamudurthy V, et al. Biomarkers in colorectal cancer screening. *J Gastrointest Dig Syst*. 2016;6:389.
31. Bhagat V and Wanebo H. An overview of colorectal cancer screening. *J Carcinog Mutagene*. 2015;6:243.
32. Moattar M, et al. Practical application of health belief model to enhance the uptake of colorectal cancer screening. *J Community Med Health Educ*. 2014;4:297.
33. Heather BF, et al. Understanding gender, race and ethnicity in colorectal cancer screening. *health care current reviews*. 2015;3:131.

34. Levin B, et al. Screening and surveillance for the early detection of colorectal cancer and adenomatous polyps, 2008: A joint guideline from the American cancer society, the US multi-society task force on colorectal cancer and the American college of radiology. *CA Cancer J Clin.* 2008;58:130-160.
35. Mandel JS, et al. Reducing mortality from colorectal cancer by screening for fecal occult blood. Minnesota colon cancer control study. *N Engl J Med.* 1993;328:1365-1371.
36. Jin P, et al. Combined fecal transferrin test and immuno fecal occult blood test for detecting colorectal cancer and advanced adenoma in asymptomatic and symptomatic populations. *J Cancer Sci Ther.* 2012;4:243-248.
37. Turner J, et al. Sigmoid perforation during CT colonography in a patient with an inguinal hernia and concomitant finding of a right-sided colon cancer. *J Gastrointest Dig Syst.* 2016;6:378.
38. Saltz LB, et al. Irinotecan plus fluorouracil/leucovorin for metastatic colorectal cancer: A new survival standard. *Oncologist.* 2001;6:81-91.
39. Turner N, et al. Primary tumor resection in patients with metastatic colorectal cancer is associated with reversal of systemic inflammation and improved survival. *Clin Colorectal Cancer.* 2015;14:185-191.
40. Timofeiov S, et al. Conversion rate to resectability in colorectal cancer liver metastases: Need for criteria adapted to current therapy. *Journal of Surgery.* 2015;11:323-336.
41. Niccolai E and Amedei A. Vaccine immunotherapy strategies in colorectal cancer treatment. *Single Cell Biol.* 2012;1:102.
42. Inoue D, et al. CD133-positive status predicts better prognosis in metastatic colorectal cancer patients treated with cetuximab. *J Cytol Histol.* 2013;5:202.
43. Lenz HJ, et al. Multicenter phase ii and translational study of cetuximab in metastatic colorectal carcinoma refractory to irinotecan, oxaliplatin and fluoropyrimidines. *J Clin Oncol.* 2006;24:4914-4921.
44. Zhang B, et al. A potential administration-time dependent effect of bevacizumab in improving overall survival and increasing metastasis in metastatic colorectal cancer. *Chemotherapy.* 2013;2:108.
45. Hochster HS, et al. Safety and efficacy of oxaliplatin and fluoropyrimidine regimens with or without bevacizumab as first-line treatment of metastatic colorectal cancer: results of the tree study. *J Clin Oncol.* 2008;26:3523-3529.
46. Giantonio BJ, et al. Bevacizumab in combination with oxaliplatin, fluorouracil and leucovorin (FOLFOX4) for previously treated metastatic colorectal cancer: results from the eastern cooperative oncology group study e3200. *J Clin Oncol.* 25:1539- 1544.
47. Cheng YH, et al. Cancer/testis (ct) antigens, carcinogenesis and spermatogenesis. *Spermatogenesis.* 2011;1:209-220.
48. Fischer M, et al. Anti-dll4 inhibits growth and reduces tumor-initiating cell frequency in colorectal tumors with oncogenic kras mutations. *Cancer Res.* 2011;71:1520-1525
49. Sharma P, et al. Contemporary management of non-appendicular mucinous and signet cell colorectal cancer in community setting. *Surgery Curr.* 2015;5:228.
50. Fuchs CS, et al. Randomized, controlled trial of irinotecan plus infusional, bolus or oral fluoropyrimidines in first-line treatment of metastatic colorectal cancer: results from the bicc-c study. *J Clin Oncol.* 2007;25:4779-4786.
51. Ichihara H, et al. Negatively charged cell membranes-targeted highly selective chemotherapy with cationic hybrid liposomes against colorectal cancer *in vitro* and *in vivo*. *J Carcinog Mutagen.* 2016;7:267.
52. Bandar MHA, et al. The current scope of robotic surgery in colorectal cancer. *Adv Robot Autom.* 2015;S2:002.

53. Yonemura Y, et al. Risk factors for recurrence after complete cytoreductive surgery and perioperative chemotherapy in peritoneal metastases from gastric cancer. *J Integr Oncol* 2016;5:167.
54. Yonemura Y, et al. A new bidirectional intraperitoneal and systemic induction chemotherapy (BISIC) for the peritoneal metastasis from gastric cancer in neoadjuvant setting. *integrative cancer science and therapeutics. Integr Cancer Sci Therap.* 2014;1:26-29.
55. Matsusaka S, et al. Circulating tumor cells as a surrogate marker for determining response to chemotherapy in japanese patients with metastatic colorectal cancer. *Cancer Sci.* 2011;102:1188-1192.
56. Polenz C, et al. Adjuvant chemotherapy for colorectal cancer–timing is everything. *Chemotherapy.* 2013;2:110.
57. Baxter NN, et al. Association of colonoscopy and death from colorectal cancer. *Ann Intern Med.* 2009;150:1-8.
58. Goi T, et al. Retrospective analysis of chemotherapy-induced nausea and vomiting (cinv) in colorectal cancer patients treated with antiemetics. *J Palliative Care Med.* 2012;S1:006.
59. Lumpkins CY, et al. Racial/ethnic variations in colorectal cancer screening self-efficacy, fatalism and risk perception in a safety-net clinic population: Implications for tailored interventions. *J Community Med Health Educ.* 2013;3:196.
60. Wang L, et al. Systemic chemotherapy with and without anti-egfr antibody in the first-line treatment of metastatic colorectal cancer. *J Cell Sci Ther.* 2012;3:124.
61. Yoshida Y. Port free chemotherapy for recurrent or metastatic colorectal cancer. Is port really necessary? *J Cancer Sci Ther.* 2012;4:iv-iv.
62. Katsuno G, et al. Incisionless laparoscopic colectomy for colorectal cancer “hybrid notes technique applied to traditional laparoscopic colorectal resection”. *J Gastroint Dig Syst.* 2011;S6:001.
63. Ogawa T, et al. Immunotherapy targeting cancer stem cells of human colorectal cancer. *J Gastroint Dig Syst.* 2013;S12:014.
64. Brierley GV, et al. Circulating levels of the wnt antagonist dkk-3 as a diagnostic marker for colorectal cancer. *J Mol Biomarkers Diagn.* 2013;S8:008.
65. Fajardo LL, et al. Clinical and radiological considerations for incorporating computed tomographic colonography into colorectal cancer screening programs. *J Med Diagn Meth.* 2013;2:109.
66. Lam M, et al. Systemic inflammation – impact on tumor biology and outcomes in colorectal cancer. *J Clin Cell Immunol.* 2015;6:377.
67. McMillan DC, et al. Systemic inflammatory/ response predicts survival following curative resection of colorectal cancer. *Br J Surg.* 2003;90:215-219.
68. Stein A, et al. Current standards and new trends in the primary treatment of colorectal cancer. *European Journal of Cancer.* 2011;47:S312–s314.
69. Ungari AQ, et al. Cost evaluation of metastatic colorectal cancer treatment in the Brazilian public healthcare system. *J Integr Oncol.* 2015;4:136.
70. Lochhead P, et al. Etiologic field effect: reappraisal of the field effect concept in cancer predisposition and progression. *Mod Pathol.* 2014;28:14-29.
71. Torre LA, et al. Global cancer statistics, 2012. *CA Cancer J Clin.* 2015;65:87-108.
72. Ota S, et al. Quality improvement in external radiation therapy using a departmental incident-reporting system and multidisciplinary team efforts. *J Nucl Med Radiat Ther.* 2015;6: 243.
73. Baichoo E and Boardman LA. Genetics of young onset colorectal cancer. *Genetics.* 2013;3:124.

74. Bandipalliam P. Syndrome of early onset colon cancers, hematologic malignancies & features of neurofibromatosis in hnpcc families with homozygous mismatch repair gene mutations. *Familial Cancer*. 2005;4:323-333.
75. Kempers MJ, et al. Risk of colorectal and endometrial cancers in epcam deletion-positive lynch syndrome: A cohort study. *Lancet Oncol*. 2011;12:49-55.
76. Ohhara Y, et al. Circulating tumor cells as prognostic marker in japanese patients with kras wild-type metastatic colorectal cancer receiving panitumumab after progression on cetuximab. *J Cytol Histol*. 2013;5:204.
77. Barone M, et al. Estrogens, phytoestrogens and colorectal neoproliferative lesions. *Genes Nutr*. 2008;3:7-13.
78. Diaz Jr LA, et al. The molecular evolution of acquired resistance to targeted egfr blockade in colorectal cancers. *Nature*. 2012;486:537-540.
79. Figueredo A, et al. Adjuvant therapy for stage ii colon cancer: A systematic review from the cancer care Ontario program in evidence-based care's gastrointestinal cancer disease site group. *J Clin Oncol*. 2004;22:3395-3407.
80. Ira S. Impact of intracellular signaling in colorectal cancer (CRC). *J Gastroint Dig Syst*. 2012;2:e109.
81. Tanaka T and Tamura K. Recent advances in molecular targeted therapy for advanced colorectal cancer and non-small cell lung cancer. *J Phys Chem Biophys*. 2012;2:108.
82. Roy S, Majumdar APN. Cancer stem cells in colorectal cancer: Genetic and epigenetic changes. *J Stem Cell Res Ther*. 2012;S7:006.
83. Yochum GS. AXIN2: tumor suppressor, oncogene or both in colorectal cancer? *J Cancer Sci Ther*. 2012;4:xii-xiii.
84. Klein and Sarah. 12 famous faces touched by colorectal cancer. 2012.
85. Zaenker KS, et al. A specific mistletoe preparation (iscador-qu®) in colorectal cancer (crc) patients: more than just supportive care? *J Cancer Sci Ther*. 2012;4:264-270.
86. Benharroch D and Ariad S. Mild dehydration - possible association with bladder and colorectal cancers - a review. *J Food Process Technol*. 2012;3:142.
87. Lupinacci RM, et al. Hilar lymph node involvement in colorectal cancer liver metastases – an overview. *J Gastroint Dig Syst*. 2011;S6:002.
88. Tovar JR, et al. Hereditary nonpolyposis colorectal cancer (Lynch Syndrome). \*DVWURLQW'LJ6\VW. 2012;S6:003.
89. Wang S, et al. Enrichment and selective targeting of cancer stem cells in colorectal cancer cell lines. *Human Genet Embryol*. 2012;S2:006.
90. Suman S and Datta K. Colorectal carcinogenesis and animal models. *J Carcinogene Mutagene*. 2012;3:e104.
91. Cidón EU. What is the optimal treatment for metastatic colorectal cancer? controversial points. *J Cancer Sci Ther*. 2011;S4:003.
92. Gill RS, et al. Combined hepatic and inferior vena cava resection for colorectal cancer. *Surgery*. 2011;S4:001.
93. Simpson JAD, et al. Single dose preoperative administration of intravenous iron corrects iron deficiency anaemia in colorectal cancer. *J Blood Disord Transfus*. 2010;1:101.
94. Eliana K, et al. Colorectal cancer: A pathology of the colon-rectum and a disease of the genome. *Intern Med*. 2013;3:120.
95. Kozicky L, et al. Inflammation plays multiple roles in colorectal cancer. *J Gastroint Dig Syst*. 2013; 3:127.
96. Parkin DM, et al. The fraction of cancer attributable to lifestyle and environmental factors in the UK in 2010. *British Journal of Cancer*. 2011;105:S77-S81.

97. Campos FG, et al. Diet and colorectal cancer: Current evidence for etiology and prevention. *Nutricion Hospitalaria*. 2005;20:18-25.
98. Patidar P and Bhojwani J. Identification and pattern analysis of snps involved in colorectal cancer. *J Stem Cell Res Ther*. 2013;3:144.
99. Merika E, et al. Review. Colon cancer vaccines: An update. *In Vivo*. 2010;24:607-628.
100. Desch CE, et al. Colorectal cancer surveillance: 2005 update of an american society of clinical oncology practice guideline. *J Clin Oncol*. 2005.