## Annex G: Pathway for the Z Benefits for Colorectal Cancer

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# Pathway for the Z Benefits for Colorectal Cancer

Referred to/ Visits Cancer Clinic for cancer diagnosis verification

A change in bowel habit, whether constipation or diarrhea, direct suspicion of colorectal cancer

COLON: A tumor in the ascending colon may present with microcytic anemia, occult blood in the stool, or a palpable mass in the right lower quadrant. A tumor in the descending colon presents with hematochezia, obstructive symptoms and small caliber stools. RECTUM: Lesions in the rectum present with local bleeding, pain, change in bowel habits and stool caliber, and then tenesmus.

COLON: Colonoscopy is a very accurate diagnostic tool for detecting and defining primary colon lesions; once a colon mass is seen, biopsy can be done via colonoscopy.

RECTUM: Most cancers can be detected by simple divital exam (65-80%). Once discovered, proctosismoidoscopy with biopsy

Biopsy (+) Referred to/ Visits Cancer Clinic for pre-treatment evaluation Chest x-ray, ultrasound abdomen negative for metastasis

> Z Package Considers ONLY: Colon Stage M0, N0-N1, any T (0-IIIB) Rectum Stage M0, N0-N2, any T (I-III)

COLON: CT scan of whole abdomen (preferably with contrast), CEA, FBS, SGPT, AP, CBC, Blood typing, Albumin, Creatinine, CXR (PA-L), ECG as baseline. CP clearance, prothrombin time, and other services mentioned in the Z package as needed RECTUM: CTscan of whole abdomen and pelvis (with contrast, preferably triple contrast), Pelvic MRI, CEA, FBS, SGPT, AP, CBC, Blood typing, Albumin, Creatinine, CXR (PA-L), ECG, Endorectal ultrasound as baseline. CP clearance, Prothrombin time, and other services mentioned in the Z package as needed



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Disease Stage	Surgery (Done by Colo-Rectal Surgeons)	Risk Category	Drug Therapy Regimen (Done by Medical Oncologists)	Radiotherapy (Done by Radio- Oncologists)	Support Drugs	Diagnostics/ Treatment Response Monitoring		
B. Cancer appropriate for resection								
Resectable, non- obstructing (T1-3 N1 M0)	Colectomy with enbloc removal of regional LN	LVI negative or Low grade	For low risk: Cape2000 OR FU500/FA500	No radiotherapy	Antibiotics, anti- emetics, pain relievers, filgrastim, blood support (with x- matching, typing, processing)	PE, Symptomatology, weight, CEA, CXR PAL, UTS abdomen (CT scan if high suspicion), SGPT, Creatinine Colonoscopy after 1 year then as indicated		
Resectable, non- obstructing (T1-3 N1 M0)	Colectomy with enbloc removal of regional LN	LVI positive or High grade	For intermediate to high risk: CapeOX Or FOLFOX 4	No radiotherapy				
Resectable, obstructing (T4, N0-1, M0)	One-stage colectomy with en- bloc removal of regional LN Or Resection with diversion Or Stent, followed by colectomy with en bloc removal of regional LN	High risk	CapeOX Or FOLFOX 4	No radiotherapy				
	Or Diversion followed by colectomy with en bloc removal of regional LN							
C. Medically inoperable (T1 N0 M0/ Significant medical co- morbidities)	No definitive surgery		Cape2000 OR FU500/FA 500	No radiotherapy	Antibiotics, anti- emetics, pain relievers, filgrastim, blood support (with x- matching, typing, processing)	PE, Symptomatology, weight, CEA, CXR PAL, UTS abdomen (CT scan for high suspicion), SGPT, Creatinine Colonoscopy after 1 year then as indicated		
Medically inoperable (T2-4 N0-1 M0)	Diversion as needed		CapeOX Or FOLFOX 4	No radiotherapy				

Disease Stage	Surgery (Done by Colo-Rectal Surgeons)	Risk Category	Drug Therapy Regimen (Done by Medical	Radiotherapy (Done by Radio- Oncologists)	Support Drugs	Diagnostics/ Treatment Response Monitoring
RECTUM			Olicologists)			
Appropriate for	resection					
T1-2 N0	Transabdominal resection Or Transanal excision if appropriate	Low Risk: pT1-2 N0M0 High Risk: pT3N0M 0/ pT1- 3N1-2	No chemotherapy Adjuvant Chemotherapy: Cape2000 Or CapeOX Or FU500/FA500 Or FOLFOX4 Followed by Concurrent Chemo- Radiotherapy: Cape825RT Or FU400/	No radiotherapy Concurrent Chemotherapy RT (NOTE 4)	Antibiotics, anti- emetics, pain relievers, filgrastim, blood support (with x- matching, typing, processing)	PE, Symptomatology, weight, CEA, CXR PAL, UTS abdomen (MRI in high suspicion), SGPT, Colonoscopy after 1 year then as indicated (NOTE 7)
T3N0 or anyT, N1-2	Trans abdominal resection	High Risk	FA20RT Cape825 RT Or FU400/ FA20RT FOLLOWED BY: Cape2000 Or Cape0X Or FU500/FA500 Or FU500/FA500 Or FOLFOX4	Pre-operative Cape825 RT Or FU400/ FA20RT (NOTES 5 & 6)		
A. Unresecta ble, T4M0	Pre-op ChemoRT, then resect if possible	High Risk	Cape825RT Or FU400/ FA20RT FOLLOWED BY: Cape2000 Or Cape0X Or FU500/FA500 Or FOLFOX4	Pre-operative Cape825RT Or FU400/ FA20RT		

Disease Stage	Surgery (Done by Colo-Rectal Surgeons)	Risk Category	Drug Therapy Regimen (Done by Medical Oncologists)	Radiotherapy (Done by Radio- Oncologists)	Support Drugs	Diagnostics/ Treatment Response Monitoring
B. Medically in- operable (T1 N0 M0/ Significan t medical co- morbiditi es)	No definitive surgery	Low Risk	Cape825 RT Or FU400/ FA 20RT	Cape825RT Or FU 400/FA 20RT		
Medically in- operable (T2-4 N0-1 M0)	Diversion as needed	High Risk	Cape825RT Or FU400/ FA20RT FOLLOWED BY: Cape2000 Or CapeOX Or FU500/FA500 Or FOLFOX4	Cape825RT Or FU400/ FA20RT		

#### Note 1: Prognostic factors

- High Risk (Genetics): First-degree relatives of patients with diagnosed adenomas or invasive carcinoma are at increased risk for colorectal cancer. Colon cancer patients, especially those 50 years or younger and those with suspected hereditary non-**polyposis** colon cancer (HNPCC), familial adenomatous polyposis (FAP) and attenuated FAP should be counselled regarding family history
- **Colon** cancer patients who are high risk for systemic recurrence after colon resection are those with histological grade 3-4, lymphatic/vascular invasion, and/or bowel obstruction.
- Probability for rectum cancer to recur is relatively low if: 1) < 30 % circumference of bowel, 2) < 3 cm in size, 3) margin clear (3 > mm), 4) mobile, non-fixed, 5) within 8 cm of anal verge, 6) T1 or T2, 7) fragmented polyp, 8) no lymphovascular or perineural invasion, 9) well to moderately differentiated, and or 10) no evidence of lymphadenopathy on pretreatment imaging.

### Note 2: Surgery

Colectomy:

- LNs at the origin of feeding vessels should be identified for pathologic exam
- Clinically +LNs outside the field of resection that are considered suspicious should be biopsied or removed, if possible
- Positive LNS left behind indicate an incomplete (R2) resection
- A minimum of 12 LNs need to be examined to establish N stage
- Resection needs to be complete to be considered curative (R0)

Conversion to resectable disease:

- Re-evaluate for resection one (1) month after pre-op chemotherapy/ chemoradiotherapy
- When considering whether disease has been converted to resectable, all original sites should be amenable to resection
- Pre-operative chemotherapy regimens with high response rates should be considered for patients for potentially convertible disease.

Optimal time between surgery and pre-operative chemo-radiotherapy:

- There may be benefits in prolonging the interval between chemoradiotherapy and surgery beyond the 6 to 8 weeks that is commonly practiced (Foster JD et al. Dis Colon Rectum, 2013).
- Delaying surgery until the 15th or 16th week after the start of CRT (10-11 weeks from the end of CRT) seemed to result in the highest chance of a pCR (Sloothaak DA et al. Br J Surg, 2013).

Colostomy reversal:

- The reversal operation (2<sup>nd</sup> surgery) is usually done for early stage cancers when the patient is in good health without evidence of cancer disease and fully recovered from the effects of the colostomy formation operation, as well as chemotherapy. This will usually be at least 12 weeks or more after the initial surgery, or at least 6-8 weeks from last chemotherapy/ chemo-radiotherapy cycle.
- There's no time limit for having the stoma reversed and some people may live with their colostomy for several years before it is reversed.
- In some cases, reversing a colostomy may not be recommended. For example, if the anal sphincter muscles were damaged after surgery.

## Note 3: Chemotherapy Regimens:

- **Cape1250**: Capecitabine 1250 mg/m<sup>2</sup> 2x day from Day 1 to Day 14 every 3 weeks x 8 cycles
- **Cape2000**: Capecitabine 2000 mg/m<sup>2</sup> 2x day from Day 1 to Day 14 every 3 weeks x 6 cycles
- **CapeOX**: Oxaliplatin 130 mg/m<sup>2</sup> on Day 1 plus capecitabine 850 mg/m<sup>2</sup> 2x day from Day 1 to Day 14 every 3 weeks x 6 cycles
- **FU500/FA200**: Fluorouracil 500 mg/m<sup>2</sup> once a week x 6 weeks plus Folinic acid 200 mg/m<sup>2</sup> once a week x 6 weeks cycle to be repeated every 8 weeks for 4 cycles
- FU500/FA500: Folinic acid 500 mg/m<sup>2</sup> IV plus Flourouracil 500 mg/m<sup>2</sup> on Days 1, 8, 15, 22, 29, 36 every 8 weeks for 6 cycles
- FOLFOX 4: Oxaliplatin 85 mg/m<sup>2</sup> on Day 1 plus Folinic acid 200mg/m<sup>2</sup> on Day 1 and Day 2 plus Fluorouracil 400 mg/m<sup>2</sup> IV bolus followed by 600 mg/m<sup>2</sup> IV infusion on Day 1 and Day 2 every 2 weeks cycle for 6 cycles

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### Note 4: Surgery Adjuvant Chemotherapy Chemo-RT Regimens

- Adjuvant FU500/FA500 or FOLFOX4
  - FOLLOWED BY FU440/FA20RT: FU 400 mg/m<sup>2</sup> plus FA 20 mg/m<sup>2</sup> for 4 days during Weeks 1 and 5 of radiotherapy
- Adjuvant Cape2000 or CapeOX
  - FOLLOWED BY Cape825RT: Capecitabine 825 mg/m<sup>2</sup> 2x day for 5 days of radiotherapy x 5 weeks

#### Note 5: Pre-op Chemo-RT Regimens Surgery Adjuvant Chemotherapy:

- **FU440/FA20RT**: FU 400 mg/m<sup>2</sup> plus FA 20 mg/m<sup>2</sup> for 4 days during Weeks 1 and 5 of radiotherapy
  - o FOLLOWED BY Adjuvant FU500/FA500 or FOLFOX4
- Cape825RT: Capecitabine 825 mg/m<sup>2</sup> 2x day for 5 days of radiotherapy x 5 weeks
  FOLLOWED BY Adjuvant Cape2000 or CapeOX

Note 6: All patients who received pre-op chemoradiation and were down-staged must receive systemic adjuvant chemotherapy.

<u>Note 7</u>: Minimum surveillance work-up aside from complete physical exam (plus colostomy site), symptom & weight monitoring, are CEA, chest x-ray PA-L and UTS of whole abdomen (CTscan if highly suspect) every 4-6 months during the 1<sup>st</sup> year; colonoscopy within one year.

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