

Liver Transplantation for Metastatic Colorectal Cancer Protocol University of Cincinnati

Inclusion Criteria

Patients can be considered for liver transplantation for metastatic colorectal cancer (mCRC) if the following criteria are met:

Patient specific factors

- Good performance status, ECOG 0 or 1
- Meet standard liver transplant inclusion criteria (cardiopulmonary, financial, psychosocial)

Primary diagnosis

- Histological diagnosis of colon/rectal adenocarcinoma
- BRAF wild type, MSI stable
- RAS mutations considered if other favorable biological factors are present
- At least one year from time of CRC diagnosis to time of listing for liver transplantation

Treatment of primary CRC

- Standard surgical resection procedure of primary tumor with adequate resection margins, including circumferential resection margins (CRM) of at least ≥ 2 mm for rectal primary (R0 resection)
- No evidence of local recurrence by colonoscopy within 12 months of listing

Evaluation of extrahepatic disease

- No signs of extrahepatic disease or local recurrence, based on CT/MRI (chest, abdomen and pelvis) and/or PET scan within one month of listing. *(Addition of PET scan at discretion of treating oncologist).*

Evaluation of hepatic disease and prior systemic/liver directed treatment

- Received first-line chemotherapy
- Relapse of liver metastases after second liver resection or liver metastases not eligible for curative resection
- No hepatic lesion should be greater than 10 cm before start of chemotherapy
- Must have stability or regression of disease with systemic and/or locoregional therapy

Management of Synchronous Disease

- Must meet all above criteria for consideration with the exception of treatment of primary CRC
- Patient evaluated by multidisciplinary team to ensure candidacy for transplant
- Colectomy performed >6 months after initial diagnosis
- Hold chemotherapy for 4 weeks prior to colectomy, consider loop ileostomy for mid to low rectal cancers.

- Resume chemotherapy 4 to 8 weeks after colectomy, once cleared by colorectal surgeon/treating oncologist
- Consider local regional therapy to PET avid hepatic lesions following colectomy during chemotherapy holiday
- Minimum of 4 months of chemotherapy after colectomy before listing for transplant

Exclusion Criteria

Patients will not be considered for liver transplantation for metastatic colorectal cancer (mCRC) if the following criteria are met:

Patient specific factors

- Weight loss >10% in last 6 months
- Other malignancies
- Known hypersensitivity to rapamycin
- Women who are pregnant or breast feeding
- Patients with hereditary CRC syndromes (FAP or Lynch Syndrome)

Primary and mCRC specific factors

- Palliative resection of primary CRC tumor
- Prior extra-hepatic disease
- Local relapse
- Patients who had not received standard pre-operative, peri-operative or post-operative treatment for primary CRC
- CEA >80 µg/L with increasing trend
- CEA >80 µg/L with decreasing trend is *relative contraindication*, liver transplant could be considered if presence of other favorable biologic factors
- Rising CEA level without radiographic evidence of disease progression or new lesion

Waitlist surveillance

- CT/MRI (chest, abdomen and pelvis) and/or PET scan with CEA every three months from listing until transplant or one of the following occurs:
 - (1) Progression of hepatic disease
 - (2) Development of extrahepatic disease

Transplant

- Conventional liver transplant operation, with allocation based on candidates native MELD score.
- Only utilize extended criteria liver allografts (elderly (>70), steatotic (>30% macro), split livers, HBV/HCV NAT +, DCD, national shares, or regional open offers) if candidate native MELD < 15. Living donor allografts can be utilized once program established.

Immunosuppression

- Standard immunosuppression regimen with conversion to mTOR inhibitor from calcineurin inhibitor at one-month post-transplant.

Post-transplant surveillance

- CT/MRI (chest, abdomen and pelvis) with CEA every three months for the first 2 years then every 6 months for up to 10 years.
- Colonoscopy – if advanced adenoma (villous polyp, polyp > 1cm or high-grade dysplasia) on pre-transplant colonoscopy, repeat in one year from last colonoscopy, otherwise repeat in three years from last colonoscopy then every five years.