



*Novel Indications
for Living-Donor
Liver Transplant*

UPMC Liver Transplant Program

UPMC
LIFE CHANGING MEDICINE

Living-Donor Liver Transplant

At UPMC, we believe that living-donor liver transplant is a first-line treatment option for patients with liver disease. Living donation allows patients to receive a transplant sooner and with improved outcomes compared to deceased-donor liver transplants.

At the UPMC Liver Transplant Program, we consider each person referred to our program. We're committed to providing liver transplant services to anyone who will benefit, including those who are high risk or who suffer from complex conditions that may not qualify for a deceased donor transplant, including:

- Alcoholic hepatitis
- HCC: Extended criteria
- Cholangiocarcinoma
- Jehovah's Witness
- Bloodless medicine or bloodless surgery
- ABO incompatible living-donor liver transplant
- Unresectable colorectal metastases
- Low/ high MELD patients
- Simultaneous liver kidney
- Re-do liver transplants
- NET and other rare tumors
- HIV recipients
- Acute liver failure

About UPMC

The UPMC Liver Transplant Program is one of the oldest and largest in the United States.

Our experts have accomplished many historical "firsts" and have pioneered and refined new therapies, giving hope to patients across the country and around the world.

When it comes to the number of living-donor liver transplants performed annually, UPMC is one of the top and most experienced programs in the country and the only center to perform more living-donor liver transplants than deceased donor transplants for the past three years.

Criteria for a Living-Donor Liver Transplant

Alcoholic Hepatitis (AH)

Inclusion Criteria:

- Patients with excessive alcohol intake (>60 g/day in men and >40 g/day in women for at least 1 year) and recent onset of jaundice and liver related complications
- The episode of AH is the first liver-decompensating event
- Patients with severe AH as determined by (MELD>20), DF > 32, non-responders to prednisolone or contraindications to corticosteroid therapy
- Non responders of conventional medical therapy (corticosteroids or pentoxifylline) after 1 week, as determined by a Lille Score of >0.45 (illemodel.com/score.asp)
- Presence of close supportive family members, partners, or friends
- Absence of severe coexisting psychiatric disorders
- Favorable transplant social worker and psychologist evaluations
- Patients with non-severe AH at admission (i.e. MELD<20) that rapidly progress to a severe form (MELD>20) will also be considered as potential candidates if the criteria of disease severity persist after 1 week
- Acceptance of having an alcohol-related problem
- Willingness to engage into a long-term alcohol counseling therapy
- Existence of a caregiver that can provide care for up to 6 weeks

Exclusion Criteria:

- Patients with previous hospitalization(s) for liver-related decompensations due to alcoholic liver disease (i.e. jaundice, variceal bleeding, edema/ascites, spontaneous bacterial peritonitis or encephalopathy) that continue to drink at any time after the first presentation
- Pre-existing chronic kidney injury (creatinine >2 mg/dL) or AKI during hospitalization requiring dialysis for more than 6 weeks
- All pre-existing and current medical conditions that are contraindications to liver transplant
- Previous failed alcohol detoxification/therapy programs
- Existence of severe coexisting psychiatric disorders (i.e. personality disorders, major depression, drug dependence, bipolar disorder, eating disorder)
- Current use of recreational drugs other than marijuana or tobacco

Extended Criteria HCC

Inclusion Criteria:

- No evidence of extrahepatic metastases
- No macrovascular invasion
- No systemic cancer related symptoms (ie significant muscle wasting and weight loss)
- No superimposed Cholangiocarcinoma
- AFP < 600
- No limits in the number and size of HCC lesions, but patients with HCC outside UCSF criteria should get targeted biopsy of the largest lesion to assess tumor biology and suitability for transplant

Exclusion Criteria:

- Targeted biopsy of the largest lesion showing poor differentiation of tumor
- Presence of extrahepatic disease and/or vascular invasion
- Poor performance status
- Any general contraindications for transplant
- Evidence of distance metastasis
- Presence of systemic cancer related symptoms
- AFP > 600

Select Patients with Unresectable Metastatic Colorectal Cancer

Inclusion Criteria:

- Histologically confirmed adenoca of the colon/rectum; primary resected with adequate margins (at least 2 cm for rectal ca)
- Primary colorectal cancer tumor stage is $\leq T4a$ or $\leq N1$
- Time from primary CRC resection to transplant is at least 6 months
- Received at least 6 to 12 weeks of chemotherapy with no evidence of disease progression
- No signs of local recurrence on colonoscopy, within the past 6 to 12 months before LT evaluation
- No signs of local or extra hepatic metastases on CT CAP/MRI/ PET CT, bone scan at time of LT evaluation
- Bilateral and non-resectable liver metastases
- No major vascular invasion
- Liver metastases; metastases isolated to liver
- Carcinoembryonic Antigen (CEA) < 100 ng/dL at time of LT evaluation
- No limit in terms of number or size of lesions
- Good ECOG performance (Eastern Cooperative Oncology Group) status: 0-1

Exclusion Criteria:

- ECOG (Eastern Cooperative Oncology Group) performance status > 2
- Diagnosis of other malignancy within the past 2 years (excluding superficial skin and cervical cancers)
- Previous or current extra hepatic metastases or local recurrence
- Any general contraindication for liver transplantation
- BRAF mutant tumors
- Presence of adult immune deficiency syndrome (AIDS)

Cholangiocarcinoma (CCA)

Inclusion Criteria:

- Unresectable hilar CCA
- Diagnosis of CCA based on a malignant appearing stricture on cholangiography and one of the following:
 - > Biopsy or cytology results demonstrating malignancy
 - > CA 19-9 greater than 100 U/mL in absence of cholangitis
 - > Aneuploidy

Exclusion Criteria:

- Extrahepatic disease, including LN involvement
- Tumor size >3 cm
- Previous attempted open biopsy or resection of tumor
- Intrahepatic metastases (contiguous intrahepatic metastases permitted)
- Vascular encasement NOT a contraindication
- Prior radiation therapy or chemotherapy
- Uncontrolled infection
- Peripheral CCA

ABO Incompatible

Inclusion Criteria:

- The liver transplant candidate must be accepted for liver transplant listing by the UPMC liver transplant committee and deemed to be acceptable living-donor liver transplant candidate
- Blood group A donors must be A1 (A2 subtype donors will be treated as ABO compatible)
- Recipients must be capable and willing to undergo the more rigorous post liver transplant monitoring including all protocol liver biopsies
- Pre-liver transplant isoagglutinin titre must be < 1:8 after adequate plasmapheresis as needed

Exclusion Criteria:

- Any other organ transplant other than liver
- Any recipient deemed not a candidate for transplant by the transplant team

HIV Recipients

Inclusion Criteria:

- Documented HIV infection (by any licensed ELISA and confirmation by Western Blot)
- Current CD4+ T-cell count $>100/\text{mm}^3$ times > 6 months.
- HIV-1 RNA < 400 for >3 months
- Patients considered for transplant must be naive either to one of the protease inhibitors (PI) or to one of the non-nucleoside reverse transcriptase inhibitors (NNRTI) for purposes of salvage therapy if required post transplant
- Willing to agree to start or re-start ARV therapy in the immediate post-operative period if not currently on ARVs secondary to intolerance caused by liver dysfunction

Exclusion Criteria:

- Any history of any AIDS-defining opportunistic infection or neoplasm, except drug susceptible candida esophagitis
- History of any neoplasm except in situ anogenital carcinoma, adequately treated basal or squamous cell carcinoma of the skin, or solid tumors treated with curative therapy and disease free for > 5 years
- Inability or unwillingness to comply with immunosuppression protocol, ARV therapy, and/or HCV monitoring and therapy if indicated
- Substance use—including alcohol, illicit drugs, or abuse of prescription narcotics
- HIV genotype or phenotype demonstrating antiretroviral resistance in 3 drug classes (nucleoside reverse transcriptase inhibitors, non- nucleoside reverse transcriptase inhibitors, and protease inhibitors)

High or Low MELD Recipients

Inclusion Criteria:

- No upper or lower limit for MELD score
- Patients with low MELD score but with clinically significant symptoms of decompensated cirrhosis, e.g., Ascites, sacropenia, PSC patients with dominant stricture, hydrothorax, debilitating HSE, HCC, difficult to manage GI bleeding, etc
- Living-donor liver transplant to be discussed with any patient disadvantaged due to the current MELD allocation system irrespective of their MELD score
- No upper MELD limit for transplant as long as they meet criteria for transplant in general and have a suitable donor

Jehovah's Witness

Inclusion Criteria:

- Must fulfill all criteria for liver transplant candidacy
- Must meet the following minimum criteria: HCT > 35, Plt > 80K, INR<2
- Must be willing to accept the use of Cell saver and venovenous bypass intraoperatively
- Must be willing to have close follow-up preoperatively and postoperatively and comply with a medical regimen to maximize potential for successful transplant (such as iron therapy, epo, etc)

Exclusion Criteria:

- Deemed "not a candidate" by the Liver Transplant Selection Committee or Live Donor Advocate based on medical, surgical, social or psychiatric criteria
- Does not meet the following minimal criteria: HCT > 35, Plt > 80K, INR<2
- Does not have a potential living donor or potential donor who is willing to accept a blood transfusion
- Will not accept Cell Saver or use of bypass intraoperatively

Older Patient Cohort

Inclusion Criteria:

- Living-donor liver transplant can be offered to older patients > 65 with good performance status
- Depends on their conditioning, and overall general functional status

Other Potential Indications

- Simultaneous liver and kidney transplant: will require two separate living donors: for kidney and liver
- Re-do liver transplants: not a contraindication as long as they meet the criteria for a liver transplant



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