TSANZ

The Transplantation Society of Australia and New Zealand

TSANZ guidance document

Liver Transplantation for Non-resectable Colorectal Liver Metastases

Version 1 – October 2025

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Disclaimer:
This document has been developed by the Liver and Intestinal Transplant Advisory Committee (LITAC) of the Transplantation Society of Australia and New Zealand (TSANZ). It serves as a common framework for the management of unresectable colorectal liver metastases as an indication for liver transplantation within Liver Transplant units across Australia and New Zealand (NZ). As the evidence in this field continues to evolve, this document will be updated to reflect local constraints and advancements. Rather than being a restrictive document, this document should be viewed as a guide that outlines general agreed-upon principles and is subject to modification as new local and international data emerge, keeping in mind that the Australian and NZ context might be different than other countries. Additionally, criteria may differ between Australia and NZ and in between Australian liver transplant units, to reflect specificities regarding population and access to treatments. Patients who are assessed for or who receive a liver graft for this indication will be audited by TSANZ via the Australia & New Zealand Liver and Intestinal Transplant Registry (ANZLITR).

Abbreviations

CLM	colorectal liver metastases
CRC	colorectal cancer
DCDD	donation after circulatory determination of death
DNDD	donation after neurological determination of death
LDLT	live donor liver transplantation
LN	lymph node
LT	liver transplantation
OS	overall survival

Background

Early Experience of Liver Transplantation for CLM

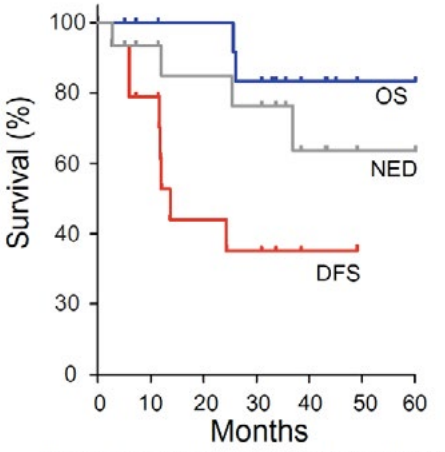
The early experience of liver transplantation (LT) for colorectal liver metastases (CLM) was not encouraging. The largest reported multi-centre series, from the European Liver Transplant Registry, reported outcome on 55 patients transplanted for non-resectable CLM between 1977 and 1995. The 5-year overall survival (OS) was only 18%. However, 44% of deaths were unrelated to tumour recurrence and the poor results, at least in part, reflect poorer outcomes overall in the early era of LT.[1] Nevertheless, these results and similar experience published by a few other single centres discouraged the allocation of scarce donor organs for this indication. Until 2020, CLM remained a contra-indication to LT in most transplant units around the world.

Recent Experience of Liver Transplantation for CLM

The group from Oslo prospectively examined the role of LT for CLM. In their initial study (Secondary Cancer; SECA I) 25 patients with non-resectable CLM were enrolled from 2006 to 2011, of whom 21 were transplanted.[2] An 5-year OS of 60% was obtained for all patients and 85% in a subset of 'low risk' patients (defined post-hoc as Oslo Clinical Risk Score 0-2). The high risk factors contributing to the Oslo score include; disease free interval < 24 months, CEA > 80µg/L, largest tumour >5.5cm and disease progression on chemotherapy.[3]

Informed by SECA I, the Oslo group went on to the SECA II study, using more restrictive entry criteria including; a minimum of 12 months from primary resection to listing, stable or chemo-responsive disease (defined as >10% response by mRECIST), some limits on tumour burden, and CEA <80ng/mL.[4] Fifteen patients were transplanted under the SECA II protocol with further improvement in outcome. Five-year OS was 85% and although 5-year disease-free survival (DFS) was only 35%, many of the recurrences (predominantly lung) were resected and nearly two thirds of patients had no evidence of disease at 5 years follow up. In SECA II, the factors associated with better outcome included Fong Clinical Risk Score 0-2[5], Oslo Clinical Risk Score 0-2, and metabolically active tumour volume (MTV) on PET scan <70cm2 measured within 90 days of transplant. Factors associated with poor outcome included elevated CEA and right sided primary tumour, consistent with observations in the non-transplant setting[6].

Figure. SECA II study from[4]



Months	0	6	12	18	24	30	36	42	48	54	60
OS	15	14	12	12	12	10	6	5	2	1	2
DFS	15	11	6	5	5	4	2	1	1	0	0
NED	15	13	11	9	9	9	5	4	2	1	1

The first randomised controlled study investigating the role of LT in the management of CLM was conducted in France by Adam et al (TransMet) with the results presented at the American Society of Clinical Oncology in 2024 and published in the Lancet[7]. This trial included non-resectable liver only patients and compared LT+ chemotherapy to chemotherapy alone, 5-year OS being the main endpoint. Of note, right-sided primary tumours and RAS mutated tumours were not excluded, although only present in small proportions (15% and 23%, respectively). All patients in the LT group had synchronous liver metastases. There were 94 patients randomised: 47 in each group. Patients randomised to the LT arm were prioritised on the deceased-donor waiting-list to receive a graft within 2 months. The protocol included post-LT chemotherapy. On intention-to-treat analysis, the 5-year OS was 57% in the LT group vs 13% with chemotherapy alone (p=0.0003). On per protocol analysis, 5y OS were 73% in the LT group vs 9%in with chemotherapy alone (p<0.0001). In those patients who received a LT, 72% experienced recurrence, of whom 46% underwent resection or ablation. At a median follow-up of 50 months, 15/36 transplanted patients (46%) had no evidence of active disease.

Figure. Overall survival in per protocol analysis from TransMet trial [7]

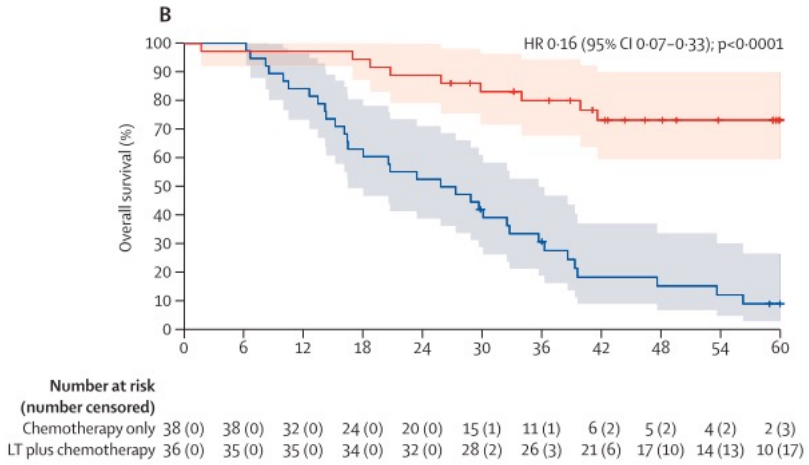
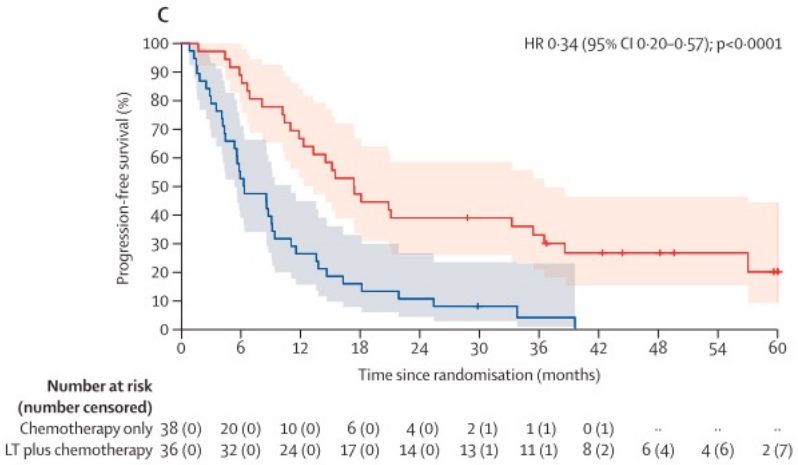


Figure. Progression-free survival in per protocol analysis from TransMet trial [7]



In summary, this recent experience appears to justify cautious optimism for the role of LT in well selected patients with non-resectable CLM, but results are markedly worse in patients with multiple adverse prognostic factors[8, 9]. The outcomes for well selected patients reported from Norway and from the TransMet trial certainly exceed the minimal listing threshold of 50% 5-year survival expectation, as recommended by the TSANZ guidelines[10], and well selected patients had similar 5-year survival to patients transplanted within HCC criteria used in Australia and New Zealand[11].

Relatively high rates of post-transplant recurrence are seen but do not seem to impact greatly on 5-year survival, and restrictive selection criteria appear to result in an acceptable proportion of patients who are either recurrence-free at 5 years or rendered disease-free by resection of lung metastases[4,7]. The only 10-year data in the modern era was reported recently from Norway[12]. They report 50% actual 10-year survival in patients with no more than 1 adverse prognostic factor (Oslo score 0-1), 33% actual 10-year survival in patients with 2 adverse factors (Oslo score 2), and zero 10-year survival in patients with more than 2 adverse factors (Oslo 3-4).

Despite some unanswered questions there is strong international interest in LT for CLM, culminating in a consensus guideline published by the International Hepato-Pancreato-Biliary Association (IHPBA) in 2021, before the results of the TransMet trial were available[13]. The aim of the guideline was to provide a framework by which LT for non-resectable CLM may be safely instituted. The guideline covers the key aspects of patient selection, evaluation of biological behaviour, graft selection and allocation, and recipient management[13].

Potential Donor Organ Sources

Several sources for grafts are potentially available for this indication. However, depending on the donor and the recipient, live donors or RAPID procedures (see below) are not always available or technically feasible, and, in order to maintain equity, it was recommended by the TSANZ LITAC that patients awaiting a LT for unresectable CLM would be able to access the deceased organ pool. In the event that a deceased donor does not become readily available, it would be appropriate for the transplant unit to explore other donor options including live donation and extended criteria donors.

Deceased donor organs

Unlike most other patients awaiting liver transplantation, patients with CLM usually do not have underlying liver disease or portal hypertension. They would therefore be suitable to receive any deceased donor graft type, including whole liver from a deceased after neurological determination of death (DNDD), split liver grafts (right or left), liver from a donor after circulatory determination of death (DCDD), and liver from an extended criteria donor. The absence of underlying liver failure and portal hypertension makes patients with CLM ideal recipients for these more marginal/ extended criteria grafts.

Adult-to-adult LDLT

LDLT using right lobe graft would be possible for patients who have a suitable right lobe donor. A major advantage of LDLT is that it enables control of the timing of transplant, thereby averting the risk of disease progression while waiting.

RAPID Procedure

The RAPID procedure[14] involves a left hepatectomy in the recipient with right portal vein ligation and transplantation of a left lateral sector graft, followed a few weeks later by the removal of the right lobe in the recipient. Although this technique might provide a suitable graft for a CLM recipient without reducing the donor pool (only applicable if there is no paediatric recipient waiting), not all CLM recipients will be suitable for this option. For example, previous left hepatectomy, or inability to transect the liver without encroaching the tumour would make it impractical. Also, it is not yet known whether the two-stage procedure has an adverse impact on tumour biology and recurrence risk.

Eligibility criteria

Eligibility criteria differ slightly across liver transplant units to reflect local practices and input from other teams involved in patient care, particularly medical oncology specialists.

Below is a summary of the main indications, absolute contraindications, and prognostic factors linked to poorer outcomes and reduced survival after liver transplantation. Depending on the clinical context and individual patient profiles, these factors—individually or combined—may constitute a contraindication to LT for CLM.

Indication

- Non-resectable colorectal liver metastases with active residual disease at the time of assessment (either stable disease or partial response), demonstrated on at least one imaging modality (MRI, CT, or PET).
- Meets general transplant suitability criteria as determined by the individual liver transplant unit.
- Previous liver resection is not a contraindication unless it creates technical barriers that make transplantation unfeasible.
- Primary tumour has been resected with clear (R0) margins in line with international oncological standards. For rectal primaries that have shown complete response to radiotherapy, surgical resection is still required before transplantation.
- Synchronous liver metastases may be considered for inclusion.

Contra-indications

- Patients that have become resectable after chemotherapy. Resectability will be decided at a multidisciplinary meeting (MDM) with Hepato-Pancreato-Biliary (HPB) surgeons, medical oncologists, and radiologists, and will be defined by the possibility of leaving enough inflow, outflow, and volume of liver parenchyma free of visible tumours.
- Any extra-hepatic metastases, to the exclusion of resectable/ablatable lung metastases or LN of the porta hepatis
- Radiological (according to RECIST criteria) or biological (rising CEA-more than 20%) progression with chemotherapy within the past 3 months before listing
- MSI high and/or MMR deficient tumours responding to treatment
- BRAF V600E mutation
- Primary tumour in situ
- Less than 6 months between the diagnosis of the CLM and the LT

Poor prognostic factors

- Right-sided primary
- BRAF mutation (exclusion of V600E)
- Other mutations (such as p53)
- Perforated primary tumour
- Undifferentiated or signet-ring cell pathology

- TNM N2 and above of the primary tumour
- Interval from diagnosis of CLM and LT below 1year
- Lung metastases
- Bulky liver disease (metabolic tumour volume on PET scan before LT more than 70cm3)
- CEA>80□□g/L at the time of diagnosis without decrease during treatment
- RAS mutation
- Positive LN in the porta hepatis (previous surgery or frozen sections at the time of LT, either systematic or on demand, at the transplant unit's discretion)
- ≥ 3 lines of chemotherapy regimens

Assessment

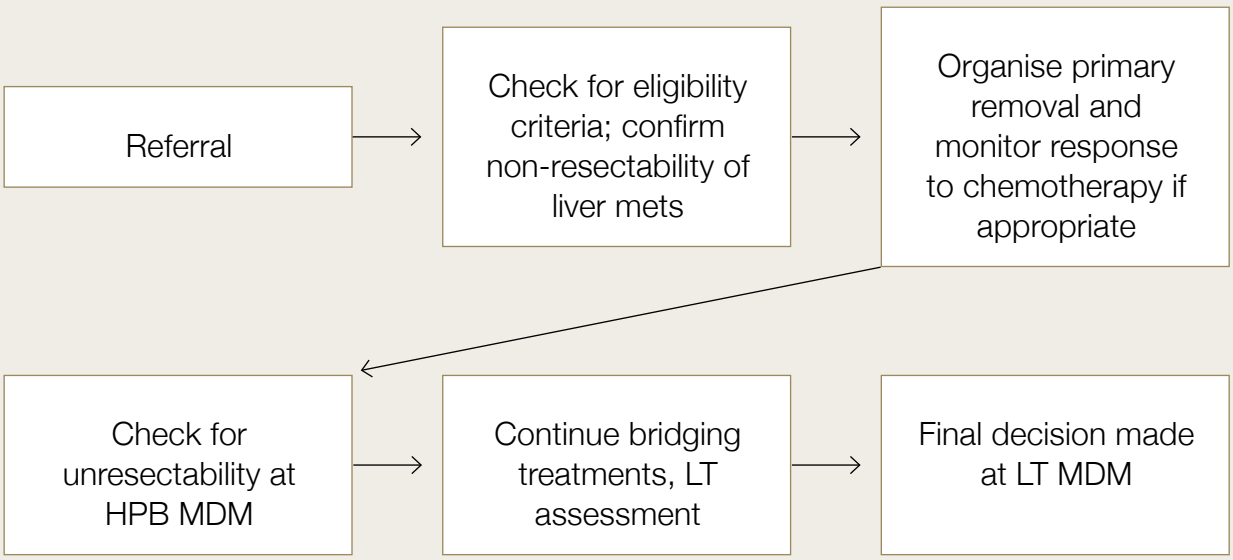
The following baseline investigations are recommended

- Histologically proven CRC with radiologically evident CLM
- Analysis of primary tumour or metastases, or both, for BRAF and RAS mutations, and MMR status
- Liver evaluation with multi-slice CT and contrast MRI
- CT CAP
- CT-PET scan
- CEA
- A complete colonoscopy should be performed within 1 year before inclusion

Re-staging investigations are undertaken 3 monthly to evaluate response to treatment and eligibility to proceed on LT pathway.

- Transplant assessment will be carried out according to local protocols.
- Local medical oncology assessment to confirm oncological criteria are met and determine treatment on waiting list.
- Surgical assessment will document suitability for the different graft options including the RAPID procedure and live donation.

Proposed referral process



Informed Consent

Patients will be informed regarding the limitations in the existing data, as well as the risks and benefits of transplantation. They need to understand and accept the procedural and medical risks, the risk of waiting list dropout if no suitable graft is available prior to documented progression. If the patient is referred to the LT unit when the primary tumour is still in situ, they should be informed that the removal of the primary is an additional procedure that would not likely be otherwise performed in the palliative pathway; and that it may cause additional morbidity with no guarantee of being listed for LT. Patients should be informed that there is a very high risk of recurrence post-transplant but that this recurrence may be amenable to treatment (half of the cases in the TRANSMET trial).

Waiting List Management

Chemotherapy

Once activated on the waiting list, patients may or may not receive further chemotherapy or maintenance chemotherapy. The maintenance chemotherapy can consist of either single agent capecitabine/infusional 5-FU or combination FOLFOX or FOLFIRI treatment. The chemotherapy can incorporate cetuximab. The decision of timing of last dose of chemotherapy before placement on the waiting-list and whether to provide maintenance chemotherapy while on the waiting-list will be individualised in consultation with medical oncology advice, considering likely waiting time, tolerance, and risk of disease progression. Practices may vary between transplant units.

Loco-regional treatments

Other loco-regional treatments may be considered to control the disease, such as selective internal radiotherapy, external beam or stereotactic radiotherapy, intra-arterial hepatic chemotherapy infusion, and trans-arterial chemoembolisation.

Re-staging

Patients will have monthly CEA and 3 monthly re-staging with CT-CAP and/or MR while active on the waiting. If these tests raise suspicion of disease progression the patient will be suspended until clarification is obtained. If an exploratory laparoscopy or laparotomy is needed, it will be performed before reactivating the patient on the waiting-list.

If new extra-hepatic disease appears, or if tumour progresses during chemotherapy, the patient will drop out from the waiting-list.

Transplantation procedure

This will be done according to local guidelines and to the type of graft available for the recipient.

The procedure should start with an exploration of the abdominal cavity and frozen biopsies of extrahepatic lesions suspicious for malignancy if they were a contra-indication to the transplantation. Routine frozen sections of the LNs of the porta hepatis will be performed at the surgeon's discretion. The presence of a back-up recipient is recommended, although this may vary according to the availability of machine perfusion.

Post-transplantation management

Post-transplant chemotherapy and immunosuppression will be determined by each transplant unit and may differ based on the patient's prior chemotherapy regimen and tolerance, the explant pathology, and local immunosuppression protocols.

Patients will undergo regular imaging after transplantation to monitor for cancer recurrence. Any recurrence will be reviewed at an MDM, and where a curative option such as surgery or ablation is feasible, it should be considered on a case-by-case basis.

References

1. Hoti E and Adam R. Liver transplantation for primary and metastatic cancers. Transpl Int. 2008 Dec;21(12):1107-17

2. Hagness et M al. Liver transplantation for nonresectable liver metastases from colorectal cancer. Ann Surg. 2013 May;257(5):800-6.

3. Dueland S et al. Survival following liver transplantation for liver-only colorectal metastases compared with hepatocellular carcinoma. Br J Surg. 2018 May;105(6) :736-742

4. Dueland S et al. Survival following liver transplantation for patients with nonresectable liver-only colorectal metastases. Ann Surg. 2020 Feb;271(2):212-218.

5. Fong Y et al. Clinical Score for Predicting Recurrence After Hepatic Resection for Metastatic Colorectal Cancer. Ann Surg. 1999 Sep;230(3):309-185.

6. Dueland S et al. Selection criteria related to long-term survival following liver transplantation for colorectal liver metastasis. Am J Transplant. 2020 Feb;20(2): 530-537.

7. Adam R et al. Liver transplantation plus chemotherapy versus chemotherapy alone in patients with permanently unresectable colorectal liver metastases (TransMet): results from a multicentre, open-label, prospective, randomised controlled trial. Lancet. 2024 Sep 21;404(10458):1107-1118.

8. Giannis D et al. The role of liver transplantation for colorectal liver metastases: A systematic review and pooled analysis. Transplant Rev (Orlando). 2020 Oct;34(4): 100570.

9. Lebeck Lee CM et al. A contemporary systematic review on liver transplantation for unresectable liver metasastases of colorectal cancer. Cancer. 2022 Jun 15;128(12): 2243-2257.

10. Clinical Guidelines for Organ Transplantation from Deceased Donors Version 1.14 – June 2025 https://tsanz.com.au/clinical-guidelines

11. Barreto SG et al. Expansion of Liver Transplantation Criteria for Hepatocellular Carcinoma from Milan to UCSF in Australia and New Zealand and Justification for Metroticket 2.0. Cancers (Basel). 2022 Jun 3;14(11):2777.

12. Solheim JM et al. Transplantation for nonresectable colorectal liver metastases - long term follow up of the first prospective pilot. Ann Surg. 2023 Aug 1;278(2):239-245.

13. Bonney GK et al. Liver transplantation for non-resectable colorectal liver metastases: the international Hepato-Pancreato-Biliary Association consensus guidelines. Lancet Gastroenterol Hepatol. 2021 Nov;6(11):933-946.

14. International consensus recommendations for the RAPID procedure in liver transplantation: The RAPID Consensus ISLS 2023 Zurich Collaborative. Int J Surg. 2025 Apr 1;111(4):2766-2772.

Version Control

TSANZ recognizes the efforts of the following clinicians who generously donated their time and expertise in creating and updating this document. This guidance document is reviewed every 2 years by relevant surgical expertise including LITAC.

Next scheduled review date: October 2027.

Version	Changes	Key Authors	Approved by	Review Date
1.0	Original Guidance Document	Dr Louise Barbier Prof Simone Strasser	TSANZ Board LITAC	31/10/2025