8.1. UNRESECTABLE COLORECTAL LIVER METASTASES

Complete resection is considered as the only true-curative treatment for CLM patients. The 5-year relative survival rate for colorectal cancer patient vary widely between 91% and 12% in stage I and IV, respectively [10]. Unfortunately, nowadays, approximately only one out of five CLM patients (stage IV of the disease) can initially be considered as potential candidates to undergo liver resection [11].

The definition of resectability of CLM changed in the course of history. In the 1970s, only scarce reports regarding liver surgery were available for CLM, and locally limited resections were mainly performed [12]. A decade later, major resections had been successfully implemented, and patient survival outcomes improved [13]. In the early 1990s, CLM resection was widely accepted and universally adopted as a treatment for patients with stage IV disease due to a reduction of perioperative mortality rates [14]. Continuous progress in surgical techniques and perioperative management completely changed the attitudes in the assessment of resectability, with some patients that once would be deemed unresectable now can be successfully treated. The arsenal of therapeutic methods has never been more extensive for stage IV CLM with the possibility of repeated resections, 2-stage hepatectomy with portal vein embolization or associated liver partition and portal vein ligation for staged hepatectomy (ALPPS) [15]. Moreover, patients with initially unresectable CLM can be scheduled for chemotherapy with the intention of down-staging the tumours to perform the liver resection in case of adequate response [17]. However, even with all the treatment modalities currently available, the majority of patients will not be able to undergo liver resection and can only be scheduled for palliative therapies. For this group of patients, it now becoming increasingly possible to select those who can be candidates for LT and who can achieve comparable survival outcomes to those treated with liver resection [9].

8.2. LIVER TRANSPLANTATION AS A TREATMENT FOR UNRESECTABLE COLORECTAL LIVER METASTASES

8.2.1. CRITERIA

The criteria for selection of CLM patients for LT proposed in 2006 (SECA-I study) [9] by Hagness et al. changed in the subsequent studies. However, the core inclusion criterion is that patients selected for LT must have unresectable CLM. The only exception to that is the experimental study arm in the study registered at clinicaltrials.gov (NCT01479608) comparing liver resection and LT patients with resectable liver lesions. The decision upon resectability should be made by the multidisciplinary team (consisting of hepatobiliary and transplant surgeons, radiologists, and oncologists). Third, the primary tumour must be previously resected with no extrahepatic metastases (except

resectable lung tumours). As for now, LT is still not widely used as a standard treatment for patients with unresectable CLMs, and there are no uniformly accepted detailed criteria regarding patients with unresectable CLM that can be treated with LT. In order to provide some insight into the factors useful in the selection process, the inclusion criteria and outcomes of the ongoing international studies must be analyzed [9, 16–19]. Until their completion, the individual assessment of patient eligibility should be performed considering the proposed criteria for patient inclusion into selected ongoing clinical studies, which are summarized in Table 8.1.

Table 8.1. Selected studies on liver transplantation for unresectable colorectal liver metastases

Study	Year started	Estimated study completion	Selected Inclusion Criteria
Norway NCT01479608 (SECA-II) [9]	2011	2027	ECOG1 score of 0 or 1 Weight loss of < 10% in the last 6 months Patient BMI2 < 30 Chemotherapy for minimum of 3 cycles with no increase in the size of lesions according to RECIST3 The absence of extrahepatic disease and recurrence None of the patients before chemotherapy can have lesions larger than 10 cm and if more than 30 lesions existed all should be less than 5 cm
France NCT02597348 (TRANSMET) [16]	2015	2027	≥ 18 and ≤ 65 years BRAF wild-type in the primary tumour or liver metastases CEA4 < 80 μg/L or a decrease ≥ 50% of the highest serum CEA levels observed during the disease A platelet count > 80,000/mm^3
Germany NCT03488953 (LIVER-T(W) O-HEAL) [17]	2018	2023	No significant comorbidities that preclude transplantation Suitable living donor The tumour burden is at least a "stable disease" Chemotherapy for a minimum of 8 weeks If all contradiction for a liver transplant will be excluded from the patient's history and all available imaging will be sent to an external review board