

## **Liver III**

### **Downstaging of hepatocellular carcinoma for liver transplantation**

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#### Down-staging of Hepatocellular Carcinoma for Liver Transplantation

Tumor down-staging, defined as a reduction of viable tumor burden by local regional therapy to meet acceptable liver transplant criteria, has garnered support in recent years and has been incorporated into the latest updated BCLC staging (1). Down-staging aims at merging expanded criteria with response to local regional therapy, serving as a tool to select a subset of patients with favorable tumor biology who would respond to down-staging treatments and do well after liver transplant. In the largest single-center experience from UCSF (2), pre-specified down-staging criteria included 1 lesion  $\leq$  8 cm, 2-3 lesions  $<$  5 cm, or 4-5 nodules all  $<$  3 cm, with total tumor diameter  $<$  8 cm, and those successfully down-staged to within Milan criteria had 5-year post-transplant survival of nearly 80%. These down-staging tumor criteria have been implemented as a national policy in the United States since 2017. These earlier results have been supported by a multicenter retrospective study (3) showing a 10-year post-transplant survival of 61% in the Milan group, 52% in the down-staged group, and only 43% for those beyond Milan without down-staging. In a multi-center prospective study from the MERITS-LT consortium (4) including 209 patients from 7 centers, the probability of successful down-staging to Milan criteria exceeded 80% within 2 years. An Italian multi-center trial (5) randomized 74 patients to liver transplant versus non-transplant therapies after initial tumor down-staging. The 5-year survival was nearly 80% in the liver transplant arm versus just over 30% among those receiving non-transplant therapy. Several studies to explore the outcomes and feasibility of down-staging in patients with higher tumor burden or “all-comers” have demonstrated a lower success rate and a higher post-transplant tumor recurrence rate. As data on down-staging continue to grow, we have also gained better insight on factors predicting inferior down-staging outcomes.