After the initial very disappointing results observed in the management of hepatocellular cancer (HCC) using liver transplantation (LT) (1), a revolution has started with the introduction of the Milan criteria (MC) (2). The very seminal paper from Mazzaferro has represented a real breakpoint respect to the past, consenting to obtain substantially similar survivals among tumoral and non-tumoral patients. However, despite the MC are connected with excellent patient survivals and low recurrence rates, only a very small percentage of HCC patients meet these so stringent criteria, with a small but not negligible percentage of MC-IN patients eventually experiencing a post-LT recurrence. As a consequence, several expanded criteria have been proposed with the intent to enlarge the population of potentially transplantable patients and to further reduce the risk for HCC recurrence: however, only the San Francisco criteria proposed by Yao (3) and the Up-to-seven Criteria proposed by Mazzaferro (4) have obtained a worldwide clinical validation. Thus, despite twenty years have passed away from their introduction, the MC still remain the cornerstone of HCC selection for LT. The reason for the enduring success of the MC is connected with the fact that (I) they are easy to use; and that (II) they perfectly fall into a sort of “grey area” in which patient survivals are excellent also when radiology underestimates the cancer. As shown by Decaens (5), MC still excellently work also when the explanted liver is taken into account, but if we step-up to the (slightly) enlarged San Francisco Criteria, survivals fall and recurrences increase. However, we know that morphology alone do not tell us the entire story. Recent publications aimed at identify new selection tools able to detect “high-risk-for-recurrence” HCC patients have focused their attention on alpha-fetoprotein modification, radiological response after loco-regional treatments and inflammatory markers (6-10). We know MC still continue doing a great job in selecting patients with high risk for recurrence. However, some of these “wicked” tumors still continue fleeing. New criteria integrating HCC morphology and biology are strongly needed with the intent to “capture” all of them.

Acknowledgements
None.

Footnote
Conflicts of Interest: The authors have no conflicts of interest to declare.

References
Levi Sandri et al. Twenty years of Milan criteria

2001;33:1394-403.


