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## Impact Of Everolimus Versus Mycophenolate Mofetil In Combination With Reduced Tacrolimus On Oncologic Outcome After Liver Transplantation For Hepatocellular Carcinoma

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**Background** : In contrast to proven renal-protective effect, benefit of using everolimus (EVR) plus reduced tacrolimus (rTAC) in respect of preventing hepatocellular carcinoma (HCC) recurrence after liver transplantation (LT) is still controversial and whether preventive effect of HCC recurrence resulted from EVR itself or by reduction of tacrolimus is not clear. There has been no head-to-head study that compared oncologic outcome between EVR+rTAC and mycophenolate mofetil (MMF)+rTAC in LT for HCC. We conducted retrospective analysis comparing those two regimens in LT for HCC, with recurrence free survival (RFS) and overall survival (OS) as primary end point.

**Methods** : A retrospective study was conducted in patients who underwent LT for HCC between January 2012 and June 2020 and maintained EVR+rTAC or MMF+rTAC for 2 years (or until HCC recurrence or death). Target trough level of rTAC was 3-7 ng/mL after the first month post-LT, and 3-6 ng/mL for EVR. Propensity score matching (PSM) was performed to ensure comparability between the two groups. RFS, OS and HCC-related death were analyzed.

**Results** : Each EVR+rTAC and MMF+rTAC group comprised of 71 patients after PSM. Number of viable tumors, sum of tumor size, differentiation, microvascular invasion rates, level of alpha-fetoprotein (AFP), and prothrombin-induced by vitamin K absence or antagonist-II (PIVKA-II) were comparable between the two groups. There was no difference in 5-year RFS between EVR+rTAC and MMF+rTAC groups (88.8% vs 84.6%, p=0.547), but patients with AFP > 100ng/mL or PIVKA-II >200ng/mL benefited from EVR use with regard to RFS and OS (p=0.047, p=0.044, respectively). EVR+rTAC group showed better 5-year OS (93.5% vs 81.5%, p=0.030), and 5-year cumulative HCC-related death was significantly lower in EVR+rTAC group than in MMF+rTAC group (1.5% vs 10.8%, p=0.049)

**Conclusions** : EVR showed benefit on OS and decreased HCC-related death compared to MMF in combination with rTAC regimen. EVR seems helpful in preventing HCC recurrence with more aggressive tumor biology presented as AFP and PIVKA-II, but its effect regarding radiologic or histologic features needs to be determined in further studies.

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