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**Impact of everolimus versus mycophenolate mofetil in combination with reduced tacrolimus in liver transplantation patients with hepatocellular carcinoma within Milan criteria**

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**Introduction:** The benefit of using everolimus with reduced tacrolimus (rTAC) in respect of HCC recurrence is still controversial and whether preventive effect of HCC recurrence resulted from everolimus or from minimization of tacrolimus is not clear. There has been no head-to-head study that compared rTAC+everolimus with rTAC+mycophenolate mofetil (MMF). We describe retrospective intention-to-treat (ITT) analysis comparing outcome of those two regimens, with HCC recurrence as primary endpoint in liver transplant (LT) recipients within Milan criteria.

**Methods:** Three hundred thirteen patients who received LT for HCC at Severance Hospital, between January 2014 and December 2020 were retrospectively reviewed. Pediatrics, retransplants, combined transplants, patients with use of cyclosporine or rapamune, and above Milan were excluded. Goal of tacrolimus blood level was 4-10 ng/mL in the first month after LT and 3-6 ng/mL thereafter. With the use of Everolimus, target level thereof was 3-5 ng/mL.

**Results:** ITT population composed of patients receiving at least 1 month of MMF and then continued MMF (rTAC+MMF, n=52) or switched to everolimus (rTAC+Everolimus, n=81). Among them, 105 patients who continued MMF or everolimus without changing regimen thereafter comprised per-protocol (PP) population. In ITT population, there was no difference in gender, age, MELD, CTP score and original liver disease between the two groups. There were no significant differences in acute rejection rate, recurrence free survival (RFS) and overall survival (OS). In PP population, 4 patients had recurrence of HCC in rTAC+MMF group and 5 patients in rTAC+Everolimus group (10.8% vs 7.4%, P=0.717). There was no significant difference in 5-year RFS nor OS between rTAC+MMF and rTAC+Everolimus group (87.7% vs 91.3%, P = 0.653; 83.2% vs 94.1%, P=0.351).

**Conclusion:** There was no significant difference in HCC recurrence rate between patients receiving rTAC+MMF or rTAC+Everolimus for HCC within Milan. Prospective studies are needed to find best strategy of immunosuppression for prevention of HCC recurrence.