MULTICENTER ANALYSIS BY THE POLISH ADULT LEUKEMIA GROUP (PALG) ON THE EFFICACY AND SAFETY OF LETERMOVIR COMBINED WITH CYCLOSPORINE OR TACROLIMUS FOR PROPHYLAXIS OF CYTOMEGALOVIRUS (CMV) REACTIVATION POST-ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Background: Letermovir is used for prophylaxis of cytomegalovirus (CMV) reactivation after allogeneic hematopoietic stem cell transplantation (alloHSCT), with dose reduction when co-administered with cyclosporine (CSA) but not tacrolimus (TAC). This multicenter retrospective study evaluated the efficacy and safety of letermovir with CSA or TAC in alloHSCT recipients.
Methods: CMV IgG-positive adults with hematologic diseases undergoing alloHSCT and receiving letermovir plus CSA or TAC were included. Outcomes were analyzed up to day +100 post-transplant.
Results: A total of 335 patients were included: 193 in the CSA group and 142 in the TAC group. Acute leukemias (60.6%) were the most common indication for transplantation. Median ages were 54.5 years (CSA) and 51.8 years (TAC). Matched unrelated donors were predominant in both groups (69.4% vs. 41.5%). CMV seronegative donors accounted for 27.6% (CSA) and 38% (TAC). Myeloablative and TBI-based conditioning regimens were used in 67.9% and 21.2% (CSA) versus 72.3% and 32.4% (TAC), respectively. Graft-versus-host disease (GVHD) prophylaxis included anti-thymocyte globulin (82.9% CSA vs. 56.3% TAC) and post-transplant cyclophosphamide (2.1% CSA vs. 41.5% TAC). There were no significant differences between CSA and TAC groups in terms of renal insufficiency (43% vs. 57%, p=0.11), relapse (6.7% vs. 9.9%, p=0.3), GvHD incidence (40.4% vs. 40.1%, p=0.96), or mortality (5.7% vs. 7%, p=0.62). CMV reactivation occurred in 7.6% (CSA) and 13.4% (TAC, p=0.06). Premature letermovir discontinuation was more frequent in the TAC

group (26.1% vs. 14%, p=0.006), mainly due to CMV reactivation (36.1%). Severe hepatotoxicity was more common with TAC (23.2% vs. 13%, p=0.01), while severe infections (grade >2) were more frequent with CSA (39.4% vs. 27.5%, p=0.02).
Conclusions: Letermovir combined with TAC was associated with higher rates of premature discontinuation, primarily due to CMV reactivation. Severe hepatotoxicity occurred more frequently in the TAC group, whereas severe infectious complications were more common in the CSA group.