P1617 CLINICAL SIGNIFICANCE OF CYTOMEGALOVIRUS DRUG RESISTANCE GENE MUTATIONS IN CYTOMEGALOVIRUS INFECTION AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION

**Topic:** 30. Infections in hematology (incl. supportive care/therapy)

**Authors:** Donglin Yang1, Jingjing Wen2,3, Ying Zhang1, Gang Li1, Yawei Zheng1, Shulian Chen1, Weihua Zhai1, Rongli Zhang1, Xin Chen1, Sizhou Feng1, Mingze Han1, Erlie Jiang1

1 Department of hematopoietic stem cell transplantation, State Key Laboratory of Experimental Hematology, National Clinical Research Center for Blood Diseases, Institute of Hematology & Blood Diseases Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Tianjin, China; 2 Department of hematology, State Key Laboratory of Experimental Hematology, Institute of Hematology & Blood Diseases Hospital, CAMS & PUMC; 3 Mianyang Central Hospital, School of Medicine, University of Electronic Science and Technology of China, Mianyang, China

**Background:** Cytomegalovirus (CMV) infection is the most important complication after allo-HSCT and threatens the prognosis of patients seriously. Currently, there are limited data on CMV drug-resistant gene mutations in CMV infection after transplantation in China.

**Aims:** In order to further understand the expression of CMV drug-resistant gene mutations in patients with poor efficacy of CMV infection in single center tertiary hematology hospital in China.

**Methods:** The clinical data of 41 patients with CMV infection after allo-HSCT were retrospectively analyzed from January 2019 to July 2021 in transplantation Center of Hematology Hospital, Chinese Academy of Medical Sciences, due to refractory and probable refractory CMV infection, who were tested for CMV resistance gene mutation. The current recommended definitions are based on Guidelines for the management of cytomegalovirus infection from ECIL 7. A total of 21 patients with AML, 8 patients with ALL, 6 patients with AA, 5 patients with MDS and 1 patients with Fanconi anemia are included. Donors were HLA haploid-identical related (N = 36), HLA-identical siblings and un-related (N = 5).

Informed consent was obtained.

**Results:** Of All 41 patients included, 1 patient (2.4%) had UL97 mutation, 19 patients (46.3%) had UL54 mutation, no patients occur simultaneously with UL54 and UL97 mutation. The overall mutation frequency was 48.8% (20/41), and all mutation types were missense mutation.

UL54 gene were detected 8 cases of T691S missense mutation (8/41, 19.5%), 3 cases of M827I missense mutation (3/41, 7.3%) and 1 case of A786V missense mutation (1/41, 2.4%). All above these 3 mutation sites had been reported, but the drug resistance significance was unknown. There were 1 site mutation (A543S) of UL97 gene and 19 site mutation of UL54 gene that had not been reported. The most common mutation site is the T691S mutation in UL54 gene. In all the 41 patients, only one patient exhibited a mutation with definite anti-CMV drug resistance significance: Q578H mutation of UL54 gene, and finally was successfully treated with twice CMV-CTL infusions (figure).

Compared with patients without UL54 mutation, patients with UL54 mutation strains had a higher proportion of CMV-DNA re positive rate in 10 days after remission of DNAemia (42.1% vs.9.5%, \( \chi^2=5.647, P=0.028 \)), and had the significantly longer complete clearance time of CMV DNAemia (40 days vs. 24 days, \( Z=2.198, P=0.027 \)).

Compared with those patients without CMV gene mutation, the patients with T691S mutation had a higher incidence in terms of CMV-DNA turned re positive in 10 days and 14 days after remission of DNAemia (71.4% vs. 19.0%, \( P=0.008 \); 71.4% vs. 9.5%, \( P=0.001 \); 71.4% vs. 9.5%, \( P=0.001 \), respectively). The median time of CMV-DNA reaching the peak was significantly later (14 days vs. 10 days, \( P=0.016 \)). The median clearance time of CMV
DNAemia was significantly longer (56 days vs. 24 days, P=0.002), and the differences were statistically significant. Compared with the non-T691s UL54 mutation, the patients with T691S mutation also had similar results.

**Summary/Conclusion:** CMV gene missense mutations were detected in 48.8% of patients infected with CMV after transplantation, most of which occurred in UL54 gene and T691S mutation is a common missense mutation. The incidence of missense mutations with clear drug resistance was low (2.4%) and might be induced by antiviral therapy. The median clearance time of CMV DNAemia in UL54 mutated patients was significantly longer, and the proportion of CMV-DNA turned re positive was increased, which might be caused by T691S mutation in UL54 gene.