Prolonged viral shedding in an immunocompromised Korean patient infected with hMPXV, sub-lineage B.1.3, with acquired drug resistant mutations during tecovirimat treatment

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Abstract

Following the worldwide surge in mpox(monkeypox) in 2022, cases have persisted in Asia, including South Korea, and sexual contact is presumed as the predominant mode of transmission, with a discernible surge in prevalence among immunocompromised patients. Drugs such as tecovirimat can result in drug-resistant mutations, presenting obstacles to treatment. This study aimed to ascertain the presence of tecovirimat-related resistant mutations through genomic analysis of the monkeypox virus isolated from a reported case involving prolonged viral shedding in South Korea. Here, tecovirimat-resistant mutations, previously identified in the B.1 clade, were observed in the B.1.3 clade, predominant in South Korea. These mutations exhibited diverse patterns across different samples from the same patient and reflected the varied distribution of viral subpopulations in different anatomical regions. The A290V and A288P mutant strains we isolated hold promise for elucidating these mechanisms, enabling a comprehensive analysis of viral pathogenesis, replication strategies, and host interactions. Our findings imply that acquired drug-resistant mutations, may present a challenge to individual patient treatment. Moreover, they have the potential to give rise to transmitted drug-resistant mutations, thereby imposing a burden on the public health system. Consequently, the meticulous genomic surveillance among immunocompromised patients, conducted in this research, assumes paramount importance.

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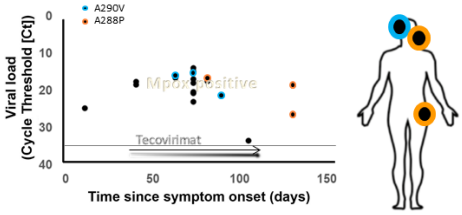


	Specimens site	Ct [F3L]	Post symptoms onset	Days to tecovirimat start
1	skin	24.78	12	-29
2	pubis	17.55	41	0
3	skin	18.45	41	0
4	Right Pubis	16.51	63	23
5	**Left forehead**	**16.24**	**63**	**23**
6	Right Pubis	14.87	73	33
7	**Left forehead**	**15.03**	**73**	**33**
8	Left arm	16.91	73	33
9	Abnomen	23.01	73	33
10	Penile	17.95	73	33
11	Right.pubis.upper	20.71	73	33
12	Left.pubis.upper	20.38	73	33
13	Left.buttok	20.63	73	33
14	**Left.pubis**	**13.93**	**73**	**33**
15	**Right.pubis**	**16.96**	**81**	**41**
16	Left.pubis	17.44	81	41
17	skin	33.49	104	64
18	**nose**	**18.64**	**129**	**89**
19	**nose**	**26.3**	**129**	**89**

Discontinuation of Tecovirimat medication

Abbreviations : Ct: Cycle threshold.

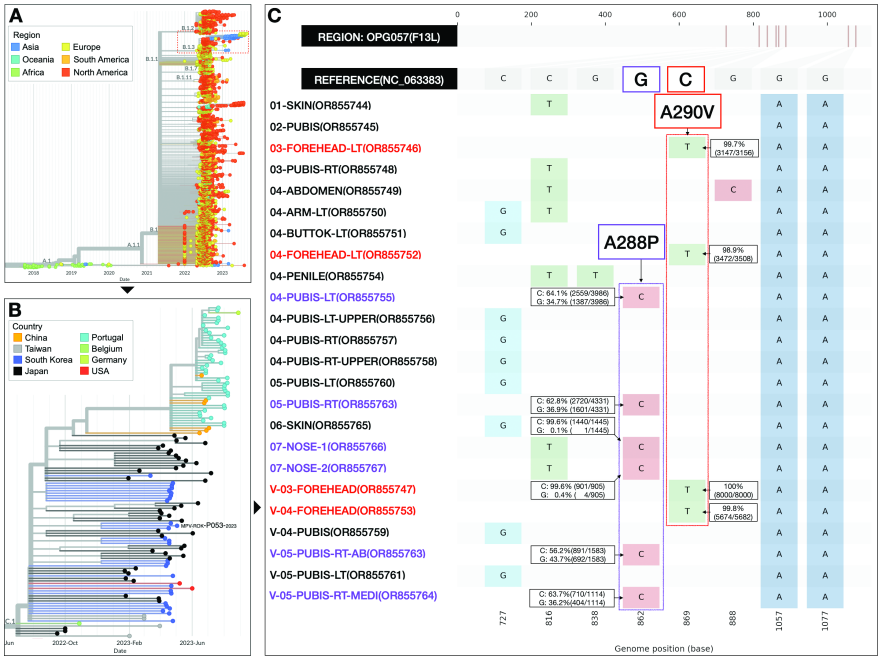
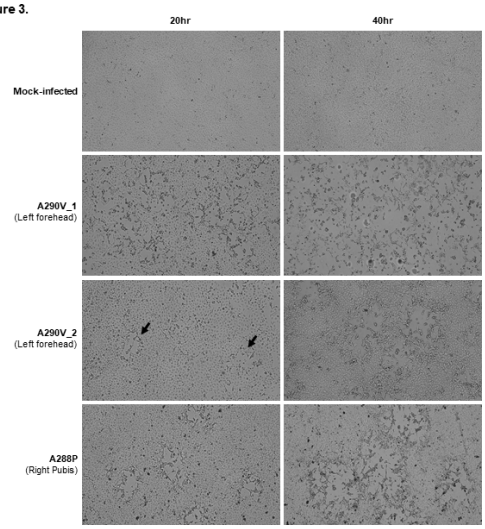


Figure 3.



Days to Tecovirimat start	Mutation	PCR Ct value (F3L)
23	A290V	14.05
33	A290V	15.41
41	A288P	15.40