Cytomegalovirus Drug Resistance by Next Generation Sequencing, Ganciclovir, Foscarnet, Cidofovir, Maribavir, and Letermovir

Last Literature Review: May 2025 Last Update: May 2025

Cytomegalovirus (CMV) is a common infection among both children and adults that is generally asymptomatic in infected immunocompetent children and adults, but can lead to serious complications in neonates, pregnant individuals, immunocompromised individuals, and transplant recipients.[1] Next generation sequencing can be used to test for CMV antiviral resistance with greater sensitivity to detect resistant subpopulations than traditional Sanger sequencing.[2] This test sequences resistance-associated mutations in the *UL27*, *UL54*, *UL56*, and *UL97* genes to assess resistance to ganciclovir, foscarnet, cidofovir, maribavir, and letermovir.

Featured ARUP Testing

Cytomegalovirus Drug Resistance by Next Generation Sequencing, Ganciclovir, Foscarnet, Cidofovir, Maribavir, and Letermovir 3004615

Method: Massively Parallel Sequencing

Provides antiviral susceptibility information for ganciclovir, foscarnet, cidofovir, maribavir, and letermovir. Intended for patients with viral load >2.6 log IU/mL.

Test Interpretation

Limitations

- Specimens with viral loads <2.6 log IU/mL may fail to amplify, thus producing indeterminate results.
- This test detects populations down to 10% of the total population, which may account for resistance interpretation differences between methods.

Evaluated Mutations

UL27 Variants							
Variant	**Cidovir**	**Foscarnet**	**Ganciclovir**	**Maribavir**	**Letermovir**	**Confirmed by Phenotyping**	**References**
A269T	–	–	–	P	–	Y	3
A406V	–	–	–	P	–	Y	3, 4
C415*	–	–	–	P	–	Y	3, 4
D534Y	–	–	–	P	–	Y	5
E22*	–	–	–	P	–	Y	3
K89N	–	–	–	S	–	Y	6
L193F	–	–	–	P	–	Y	3
L335P	–	–	–	R	–	Y	3, 7
L426F	–	–	–	P	–	Y	3
R233S	–	–	–	P	–	Y	4,5
R448P	–	–	–	P	–	Y	5
V353E	–	–	–	P	–	Y	3
W153R	–	–	–	P	–	Y	3
W362*	–	–	–	P	–	Y	3
W362R	–	–	–	P	–	Y	4

* = stop codon

del = deletion

R = "Resistant." Resistant indicates evidence of drug resistance compared with a wild-type virus.

Variant	Cidovir	Foscarnet	Ganciclovir	Maribavir	Letermovir	Confirmed by Phenotyping	References

P = "Possible Resistance." Possible resistance indicates mutations were detected with borderline-level drug resistance or conflicting resistance status reported in the literature.

S = "Sensitive." Ignored by the plugin and reported as additional variant.

— = No known resistance-association or phenotypically confirmed sensitivity to specified drug. Ignored in the analysis.

Y = "Yes." Mutation's resistance profile was confirmed by marker transfer/phenotyping experiments.

N = "No." Mutation's resistance profile has not been confirmed by marker transfer/phenotyping experiments.

UL54 Variants							
Variant	Cidovir	Foscarnet	Ganciclovir	Maribavir	Letermovir	Confirmed by Phenotyping	References
883-884ins	—	—	—	—	—	N	8
981-982del	R	R	R	—	—	Y	9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19
A505V	P	S	P	—	—	Y	8, 15
A543P	R	S	R	—	—	Y	16, 20
A692S	S	R	S	—	—	Y	11
A809V	P	R	R	—	—	Y	10, 11, 12, 15, 19, 21, 22, 23, 24, 25
A834P	R	R	R	—	—	Y	14, 15, 26
A987G	R	S	R	—	—	Y	10, 15, 19, 27, 28, 29, 30
A987V	S	R	S	—	—	Y	18, 19
C524del	R	S	R	—	—	Y	15, 31
C539G	R	S	R	—	—	Y	15, 32
C539R	R	S	R	—	—	Y	33, 34
C590F	S	R	S	—	—	Y	35
D301N	R	S	R	—	—	Y	11, 12, 15, 19
D413A	R	S	R	—	—	Y	14, 15, 36
D413E	R	S	R	—	—	Y	10, 11, 12, 14 15, 28, 37, 38
D413N	R	S	R	—	—	Y	15, 32
D413Y	R	S	R	—	—	Y	15, 39
D515E	P	P	R	—	—	Y	10, 40, 41
D515G	S	S	S	—	—	Y	11
D515Y	P	P	R	—	—	Y	15, 16, 17, 19, 41
D542E	R	S	S	—	—	Y	15, 42
D588E	S	R	S	—	—	Y	10, 28, 30
D588N	P	R	R	—	—	Y	12, 15, 23, 28, 43
D594N	S	S	S	—	—	Y	18
E303D	R	S	R	—	—	Y	15, 39
E303G	R	S	R	—	—	Y	15, 39
E756D	S	R	S	—	—	Y	11, 12, 15
E756G	S	R	S	—	—	Y	44

Variant	Cidovir	Foscarnet	Ganciclovir	Maribavir	Letermovir	Confirmed by Phenotyping	References
E756K	P	R	R	—	S	Y	11, 12, 15, 23, 28, 45, 46, 47, 48
E756Q	S	R	S	—	—	Y	12, 15, 21, 49
E951D	S	R	R	—	—	Y	15, 24
E989D	P	R	R	—	—	Y	18
F412C	R	S	R	—	—	Y	10, 12, 15, 19, 30, 50
F412L	R	S	R	—	—	Y	15, 19, 23
F412S	R	S	R	—	—	Y	15, 23, 34, 51
F412V	R	S	R	—	—	Y	10, 15, 28, 30
F595I	S	R	S	—	—	Y	15, 33, 34
G841A	R	R	R	—	—	Y	14, 15, 22
G841S	S	P	P	—	—	Y	8
G971D	S	S	S	—	—	Y	11
H600L	R	R	R	—	—	Y	44
I521T	R	S	R	—	—	Y	15, 40, 52
I722V	R	S	R	—	—	N	10
I726T	P	S	P	—	—	Y	8, 15
I726V	R	S	R	—	—	Y	8, 15
K493N	R	R	R	—	—	Y	18
K500N	R	S	R	—	—	Y	15, 33, 34
K513E	R	S	R	—	—	Y	10, 12, 15, 28, 30
K513N	R	S	R	—	—	Y	10, 12, 15, 28, 37, 53, 54
K513Q	R	S	R	—	—	Y	35
K513R	R	S	R	—	—	Y	10, 15, 19, 32
K513T	R	S	R	—	—	Y	18
K805Q	R	S	S	—	—	Y	10, 15, 21, 22, 30
L501F	R	S	R	—	—	Y	10, 28, 35, 37, 51, 55
L501I	R	S	R	—	—	Y	10, 12, 15, 28, 30, 56
L516M	S	S	S	—	—	Y	57
L516P	R	S	R	—	—	Y	17, 19
L516R	R	S	R	—	—	Y	11, 12, 15
L516W	R	S	R	—	—	Y	15, 58
L545F	R	S	R	—	—	Y	35
L545S	R	S	R	—	—	Y	10, 12, 15, 30, 33, 59
L545W	R	S	R	—	—	Y	15, 19, 23, 34
L565V	P	R	P	—	—	Y	18
L773V	R	R	R	—	—	Y	15, 32, 60

Variant	Cidovir	Foscarnet	Ganciclovir	Maribavir	Letermovir	Confirmed by Phenotyping	References
L776M	S	R	R	—	—	Y	14, 15, 61
L802M	S	R	P	—	—	Y	12, 14, 15, 21, 28, 30, 33, 43, 50, 59
L802V	S	S	P	—	—	Y	33
L862F	S	S	P	—	—	Y	33
L897P	—	—	S	—	—	Y	62
L957F	S	S	R	—	—	Y	15, 33, 34
M393K	R	R	R	—	—	N	10, 63
M393R	R	R	R	—	—	N	10, 63
M844T	S	R	S	—	—	Y	15, 64
M844V	S	R	R	—	—	Y	15, 64
N408D	R	S	R	—	—	Y	10, 12, 15, 19, 28, 30, 33, 59, 65
N408H	R	S	R	—	—	Y	35
N408K	R	S	R	—	—	Y	15, 19, 23, 26, 39
N408S	R	S	R	—	—	Y	15, 31, 66
N410K	R	S	R	—	—	Y	11, 15, 19
N495K	S	R	S	—	—	Y	14, 15, 24, 67
P488R	R	S	R	—	—	Y	32, 33
P497S	R	S	P	—	—	Y	18
P522A	R	S	R	—	—	Y	10, 15, 52
P522S	R	S	R	—	—	Y	10, 15, 19, 23, 30, 52
P522T	R	S	R	—	—	Y	35
P829S	S	S	R	—	—	Y	15, 33, 34
Q578H	R	R	R	—	—	Y	15, 19, 23, 34, 60
Q578L	S	P	P	—	—	Y	8, 15
Q783R	S	P	P	—	—	Y	24
Q807A	—	R	—	—	—	Y	21
R1052C	S	S	S	—	—	Y	68
S290R	S	R	P	—	—	Y	15, 24
S585A	S	R	S	—	—	Y	15, 33, 34
T419M	—	R	S	—	—	N	60
T503A	R	S	R	—	—	Y	35
T503I	R	S	R	—	—	Y	10, 11, 12, 14, 15
T552N	S	R	R	—	—	Y	15, 24, 33, 34
T700A	P	R	S	—	—	Y	10, 12, 15, 19, 21, 25, 30, 69
T813S	R	R	R	—	—	Y	14, 15, 22
T821I	S	R	R	—	—	Y	10, 12, 14, 15, 21, 30

Variant	Cidovir	Foscarnet	Ganciclovir	Maribavir	Letermovir	Confirmed by Phenotyping	References
T838A	S	R	S	—	—	Y	14, 15, 43
V526L	R	S	R	—	—	Y	15, 46
V715A	S	R	S	—	—	Y	15, 58
V715M	S	R	S	—	—	Y	10, 12, 15, 21, 25, 30, 49, 69
V781I	S	R	P	—	—	Y	15, 23, 28, 30
V787A	S	R	R	—	—	Y	15, 41, 48
V787E	R	R	R	—	—	Y	20, 48
V787I	—	R	—	—	—	N	12
V787L	S	R	R	—	—	Y	14, 15, 21, 33, 49, 70
V812L	R	R	R	—	—	Y	10, 12, 14, 15, 21, 33, 39, 43, 54
V823A	R	S	R	—	—	Y	18
V946L	S	R	S	—	—	Y	15, 33, 34
Y751H	R	S	R	—	—	N	10

* = stop codon

del = deletion

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UL56 Variants							
Variant	Cidovir	Foscarnet	Ganciclovir	Maribavir	Letermovir	Confirmed by Phenotyping	References
A365S	—	—	—	—	R	Y	16, 20
C25F	—	—	—	—	R	Y	16
C325F	—	—	—	—	R	Y	71, 72
C325R	—	—	—	—	R	Y	71, 72
C325W	—	—	—	—	R	Y	16, 72
C325Y	—	—	—	—	R	Y	16, 71, 72, 73
E237D	—	—	—	—	R	Y	71, 72, 74
E237G	S	S	—	—	R	Y	72, 75
F261C	—	—	—	—	R	Y	71, 72
F261L	—	—	—	—	R	Y	71, 72, 74
F261S	—	—	—	—	R	N	72
K258E	—	—	—	—	R	Y	74
L241P	—	—	—	—	R	Y	71, 73, 76, 77
L254F	—	—	—	—	R	Y	20, 77

Variant	Cidovir	Foscarnet	Ganciclovir	Maribavir	Letermovir	Confirmed by Phenotyping	References
L257F	—	—	—	—	R	Y	16, 20, 77
L257I	—	—	—	—	R	Y	71, 72
L328V	—	—	—	—	R	Y	16, 20
M329T	—	—	—	—	R	Y	71, 72, 74
N232Y	—	—	—	—	R	Y	74
N368D	—	—	—	—	R	Y	20, 77
Q204R	—	—	—	—	P	Y	74
R369G	—	—	—	—	R	Y	72, 73
R369M	—	—	—	—	R	Y	72, 73, 77
R369S	—	—	—	—	R	Y	72, 73, 76
R369T	S	S	S	—	R	Y	20, 75
S229F	—	—	—	—	R	Y	20, 77
T244K	—	—	—	—	R	Y	71, 72
T244R	—	—	—	—	R	N	72
V231A	—	—	—	—	R	Y	71, 72
V231L	—	—	—	—	R	Y	16, 71, 72, 73, 77
V236A	—	—	—	—	R	Y	16, 20
V236L	—	—	—	—	R	Y	71, 72
V236M	S	S	S	—	R	Y	16, 47, 72, 73, 77, 78
Y321C	—	—	—	—	R	Y	71, 72

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UL97 Variants							
Variant	Cidovir	Foscarnet	Ganciclovir	Maribavir	Letermovir	Confirmed by Phenotyping	References
590-593del	S	S	R	—	—	Y	10, 59
590-600del	—	—	R	—	—	N	10, 79
590-603del	—	—	R	—	—	N	10, 37
590-607del	—	—	R	—	—	N	15
591-594del	—	—	R	—	—	Y	10, 12, 80, 81

Variant	Cidovir	Foscarnet	Ganciclovir	Maribavir	Letermovir	Confirmed by Phenotyping	References
591-607del	—	—	R	—	—	Y	10, 82
595-603del	—	S	R	—	—	Y	10, 12, 70, 81, 83
597-598del	—	—	R	—	—	Y	15, 81
597-599del	—	—	R	—	—	Y	58, 81
597-603del	—	—	—	—	—	N	51
600-601del	—	—	R	—	—	Y	10, 15, 70, 81
601-602del	—	—	R	—	—	Y	15, 81
601-603del	S	S	R	—	—	Y	36, 81
A590T	—	—	R	—	—	N	10, 80, 84
A591D	—	—	R	—	—	N	10, 80, 84
A591V	—	—	R	—	—	Y	15, 16, 81
A594E	—	—	R	—	—	Y	14, 15, 85
A594G	—	—	R	—	—	Y	15, 66, 86
A594P	—	—	R	—	—	Y	10, 35, 51, 87, 88
A594S	—	—	R	—	—	Y	20, 89
A594T	—	—	R	—	—	Y	12, 15, 45, 58, 80, 82, 90, 91
A594V	—	—	R	—	—	Y	12, 13, 15, 51, 69, 79, 80, 81, 87, 90, 92
A606D	—	—	P	—	—	N	10, 80, 84
A613V	—	—	R	—	—	Y	15, 57, 66
A619V	—	—	S	—	—	Y	15, 58
A674T	—	—	S	—	—	Y	15, 93
C480F	—	—	R	R	—	Y	18, 20
C480R	—	—	R	R	—	Y	15, 94
C518Y	—	—	R	—	—	Y	15, 66, 95
C592F	—	—	R	—	—	N	10
C592G	S	S	R	—	—	Y	12, 13, 15, 18, 24, 28, 80, 81, 82, 87, 92
C603R	—	—	R	—	—	Y	14, 15, 92, 96
C603S	—	—	P	—	—	Y	14, 15, 85, 92
C603W	S	S	R	—	—	Y	10, 12, 15, 51, 53, 80, 87, 92
C603Y	—	—	R	—	—	N	10, 80, 84
C607F	—	—	R	—	—	Y	10, 15, 82, 90
C607Y	—	S	R	—	—	Y	9, 12, 15, 51, 80, 82, 97, 98

Variant	Cidovir	Foscarnet	Ganciclovir	Maribavir	Letermovir	Confirmed by Phenotyping	References
D456N	—	—	R	R	—	Y	20, 94
D605E	—	—	S	—	—	Y	13, 15, 20
E362D	—	—	R	S	—	Y	99
E596D	—	—	S	—	—	Y	15, 40
E596G	—	—	R	—	—	Y	10, 12, 15, 45, 53, 80, 82
E596Q	—	—	R	—	—	Y	35
E596Y	—	—	R	—	—	Y	15, 40
E596del	—	—	R	—	—	Y	15, 81
E655K	—	—	S	—	—	Y	15, 46
F342S	—	—	R	R	—	Y	15, 100, 101, 102
F342Y	—	—	R	R	—	Y	20, 103
G598S	—	—	R	—	—	Y	10, 12, 104
G598V	—	—	R	—	—	N	10, 84
H411L	—	—	—	R	—	Y	5, 20, 105
H411N	—	—	—	R	—	Y	5, 20, 105
H411Y	—	—	—	R	—	Y	5, 18, 20, 105
H520Q	S	S	R	—	—	Y	12, 15, 51, 80, 87, 92
I610T	—	—	R	—	—	Y	15, 40
K355M	—	—	R	R	—	Y	15, 94, 100
K355del	—	—	R	R	—	Y	100
K359E	—	—	R	S	—	Y	20, 103
K359N	—	—	R	S	—	Y	99
K359Q	—	—	R	S	—	Y	20, 103
K599E	—	—	S	—	—	Y	15, 81
K599M	—	—	R	—	—	N	10, 80
K599R	—	—	S	—	—	Y	15, 85
K599T	S	—	R	—	—	Y	10, 15, 106
K599del	—	—	R	—	—	Y	15, 81
L337M	—	—	—	R	—	Y	5, 20
L348V	—	—	S	R	—	Y	99
L397R	—	—	S	R	—	Y	5, 20, 107
L405P	—	—	R	—	—	Y	15, 85
L595F	—	—	R	—	—	Y	10, 12, 15, 80, 108
L595S	—	—	R	—	—	Y	12, 13, 15, 51, 69, 79, 80, 87, 92
L595T	S	S	R	—	—	N	10, 53, 80
L595W	—	—	R	—	—	Y	10, 12, 15, 80, 82, 87

Variant	Cidovir	Foscarnet	Ganciclovir	Maribavir	Letermovir	Confirmed by Phenotyping	References
L595del	—	—	R	—	—	Y	10, 15, 79, 80, 81, 109
L600I	—	—	S	—	—	Y	15, 85
L600del	—	—	R	—	—	Y	10, 12, 15, 45, 80, 81, 82
L634Q	—	—	S	—	—	Y	15, 82
M460I	S	S	R	—	—	Y	12, 15, 28, 51, 69, 80, 87, 92, 110
M460L	—	—	R	—	—	N	10, 84
M460T	—	—	R	—	—	Y	15, 85, 92
M460V	—	S	R	—	—	Y	12, 13, 15, 36, 40, 60, 79, 80, 87, 90, 92
M615V	—	—	S	—	—	Y	15, 96
N597D	—	—	S	—	—	Y	15, 111
N597I	—	—	R	—	—	N	10, 80
P521L	—	—	R	R	—	Y	15, 100
T409M	—	—	—	R	—	Y	5, 18, 20
T601M	—	—	S	—	—	Y	15, 81
T601del	—	—	R	—	—	Y	15, 81, 11s
V345I	—	—	S	S	—	Y	99
V353A	—	—	—	R	—	Y	3, 5, 20
V356G	—	—	R	R	—	Y	15, 100, 101
V466G	—	—	R	R	—	Y	14, 15, 96, 100
Y617H	—	—	S	—	—	Y	15, 93
Y617del	—	—	R	R	—	Y	20, 94

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