LIVTENCITY®
(maribavir) tablets 200mg

RE-DEFINING THE TREATMENT OF POST-TRANSPLANT REFRACTORY AND RESISTANT CMV[1,2]

LIVTENCITY® (maribavir) is indicated for the treatment of adults with post-transplant cytomegalovirus (CMV) infection and disease resistant, refractory or intolerant to one or more prior therapies.[1]

Ready to take a closer look at LIVTENCITY?

Explore clinical data inside

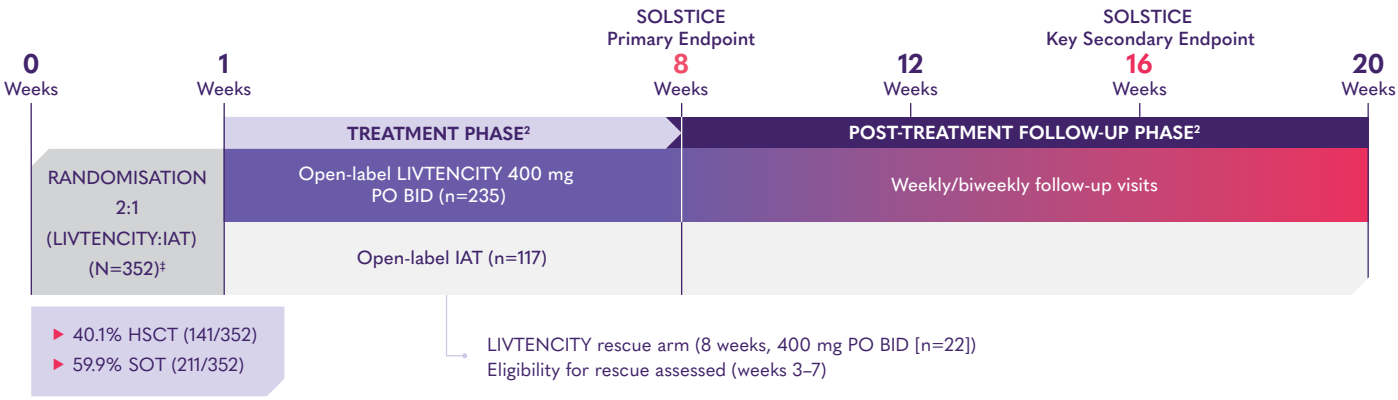
Visual metaphor.[1,2]

▼ This medicinal product is subject to additional monitoring in Australia. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse events at www.tga.gov.au/reporting-problems

Takeda

PHASE 3 SOLSTICE TRIAL DESIGN

SOLSTICE (TAK-620-303) was a multicentre, randomised, open-label, active controlled superiority trial to assess the efficacy and safety of LIVTENCITY treatment compared to investigator-assigned anti-CMV treatment consisting of monotherapy or dual therapy with ganciclovir, valganciclovir, foscarnet, or cidofovir (n=117) in 352 HSCT and SOT recipients with CMV infections that were refractory to treatment with ganciclovir, valganciclovir, foscarnet, or cidofovir, including CMV infections with or without confirmed resistance to 1 or more anti-CMV agents.[1,2]



SOLSTICE PRIMARY ENDPOINT[2]

Confirmed CMV viraemia clearance, defined as CMV DNA level below the lower limit of quantification (<137 IU/mL) in 2 consecutive tests by 5 or more days apart at the end of study week 8.*

Safety endpoints included treatment-emergent adverse events (TEAEs) and serious TEAEs (TESAEs).

SOLSTICE KEY SECONDARY ENDPOINT[2]

Achievement of CMV viraemia clearance* and symptom control† at end of Study Week 8, maintained through Study Week 16.

*CMV viraemia clearance = plasma CMV DNA concentration below the lower limit of quantification (i.e., <137 IU/mL) as assessed by COBAS® AmpliPrep/COBAS® TaqMan® CMV test at Week 8 (2 consecutive samples ≥ 5 days apart).[1]

†CMV infection symptom control was defined as resolution or improvement of tissue-invasive disease or CMV syndrome for symptomatic patients at baseline, or no new symptoms for patients who were asymptomatic at baseline.[2]

‡Stratification was done by transplant type and screening of whole blood or plasma CMV DNA level. Resistant CMV = 1 or more CMV genetic mutations associated with resistance to ganciclovir/valganciclovir, foscarnet, and/or cidofovir and meets the definition of refractory CMV infection. Refractory CMV = failure to achieve >1 log10 decrease in CMV DNA level in whole blood or plasma after a 14-day or longer treatment period with intravenous (IV) ganciclovir/oral valganciclovir, IV foscarnet, or IV cidofovir.[2]

Adapted from Avery RK, *et al* 2022.[2]

KEY INCLUSION AND EXCLUSION CRITERIA[2,3]

INCLUSION

- HSCT or SOT recipient aged ≥12 years*
- ≥2730 IU/mL (whole blood) or ≥910 IU/mL (plasma)
- CMV infection refractory to most recently administered anti-CMV agent, with or without resistance
- Screening eGFR ≥30 mL/min/1.73m2, ANC ≥1000/mm3, platelet count ≥25,000mm^3

*Although the inclusion criteria was ≥ 12 years, all patients were >18 years old.

EXCLUSION

- Resistant or refractory CMV infection due to inadequate adherence to prior anti-CMV treatment
- CMV disease with central nervous system involvement or retinitis
- Concomitant need for leflunomide, letermovir, or artesunate

Refractory is defined as documented failure to achieve >1 log10 decrease in CMV DNA level in whole blood or plasma after a 14-day or longer treatment period with intravenous (IV) ganciclovir/oral valganciclovir, IV foscarnet, or IV cidofovir.

ANC = absolute neutrophil count; **BID** = twice daily; **CMV** = cytomegalovirus; **eGFR** = estimated glomerular filtration rate; **HSCT** = haematopoietic stem cell transplant; **IAT** = investigator-assigned therapy (e.g., one or a combination of ganciclovir, valganciclovir, foscarnet, or cidofovir); **IV** = intravenous; **PO** = by mouth; **SOT** = solid organ transplant.

A CLOSER LOOK AT PATIENTS ENROLLED IN SOLSTICE

BASELINE CHARACTERISTICS[1,2§]

§ Figures vary slightly to those reported in the LIVTENCITY Product Information. Please consult the current approved Product Information for further information.

Characteristics	LIVTENCITY (n=235)	IAT(n=117)
Median age, years (range)	**57** (19–79)	54 (19–77)
Male sex, n (%)	**148** (63.0)	65 (55.6)
Solid organ transplant, n (%)*	**142** (60.4)	69 (59.0)
 Kidney†	**74** (52.1)	32 (46.4)
 Lung†	**40** (28.2)	22 (31.9)
 Heart†	**14** (9.9)	9 (13.0)
 Multiple†	**5** (3.5)	5 (7.2)
 Liver†	**6** (4.2)	1 (1.4)
 Pancreas†	**2** (1.4)	0
 Intestine†	**1** (0.7)	0
Haematopoietic stem cell transplant, n (%)‡	**93** (39.6)	48 (41.0)
CMV DNA levels category as reported by central laboratory, n (%)		
Low (<9,100 IU/mL)	**153** (65.1)	85 (72.6)
Intermediate (≥9,100 and <91,000 IU/mL)	**68** (28.9)	25 (21.4)
High (≥91,000 IU/mL)	**14** (6.0)	7 (6.0)
Confirmed symptomatic CMV infection at baseline, n (%)	**214** (91)	109 (93)
Yes§	**21** (9)	8 (7)
CMV syndrome (SOT only)§^	**10** (48)	7 (88)
Tissue Invasive disease§^	**12** (57)	1 (13)

*Based on most recent transplant type. Those classed as "multiple" had multiple organs transplanted at once.

†The denominator is the number of patients who received solid organ transplant within each treatment arm.

‡There was 1 (1.1%) autologous haematopoietic stem cell transplant in the LIVTENCITY group.

§Confirmed by Endpoint Adjudication Committee.

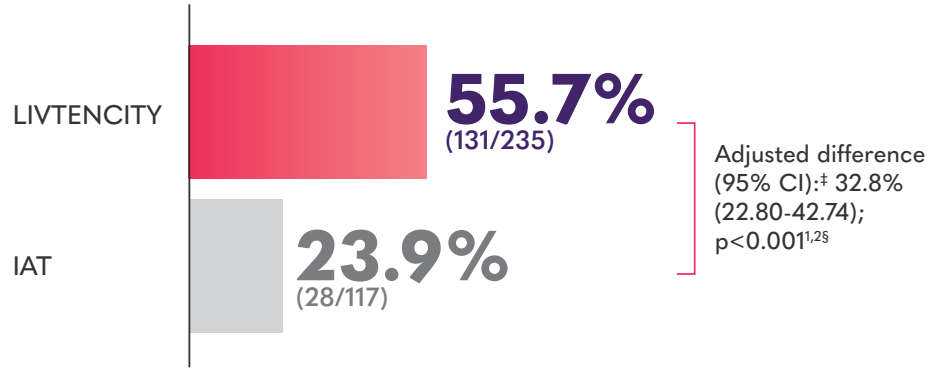
^Percentages are based on the number of patients within the category. Patients could have CMV syndrome and tissue invasive disease.

Adapted from LIVTENCITY current approved Product Information1 and Avery RK, *et al* 2022.[2]

IAT = investigator-assigned therapy (e.g., one or a combination of ganciclovir, valganciclovir, foscarnet, or cidofovir).

IN THE PIVOTAL PHASE 3 TRIAL, **LIVTENCITY DELIVERED DOUBLE THE VIRAEMIA CLEARANCE (55.7%)** COMPARED TO IAT (23.9%) – PRIMARY ENDPOINT[1,2]

Confirmed viraemia clearance* of refactory/ resistant CMV in all transplants (HSCT and SOT) at Study Week 8[1,2§]



*CMV viraemia clearance = plasma CMV DNA concentration below the lower limit of quantification (i.e., <137 IU/mL) as assessed by COBAS® AmpliPrep/COBAS® TaqMan® CMV test at Week 8 (2 consecutive samples ≥ 5 days apart).[1]

†CMV infection symptom control was defined as resolution or improvement of tissue-invasive disease or CMV syndrome for symptomatic patients at baseline, or no new symptoms for patients who were asymptomatic at baseline.[2]

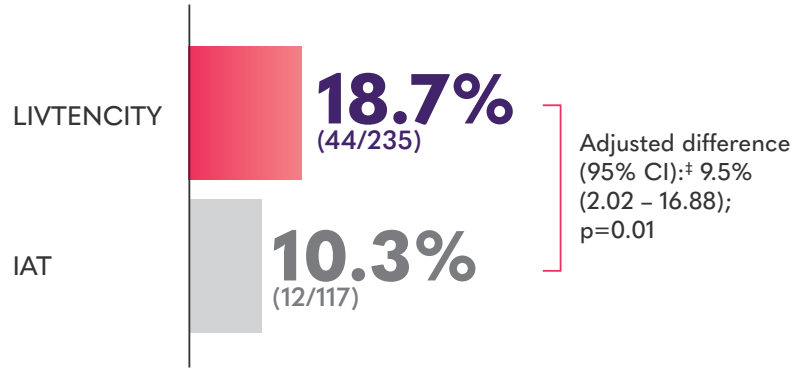
‡Cochran-Mantel-Haenszel weighted average approach was used for the adjusted difference in proportion (maribavir – IAT), the corresponding 95% CI, and the p-value after adjusting for the transplant type and baseline plasma CMV DNA concentration. Only those with both stratification factors were included in the computation.[1]

Adapted from Avery RK, *et al* 2022.[2]

IN THE PIVOTAL PHASE 3 TRIAL, **LIVTENCITY DELIVERED ALMOST DOUBLE THE VIRAEMIA CLEARANCE AND SYMPTOM CONTROL AT STUDY WEEK 8 MAINTAINED THROUGH WEEK 16 (18.7%)** COMPARED TO IAT (10.3%) – KEY SECONDARY ENDPOINT[1,2§]

§ Figures displayed vary slightly to those reported in the LIVTENCITY Product Information. Please consult the current approved Product Information for further information.

Confirmed CMV viraemia clearance* and symptom control† in all transplants (HSCT and SOT) at the end of Study Week 8, maintained through Study Week 16[1,2§]



*CMV viraemia clearance = plasma CMV DNA concentration below the lower limit of quantification (i.e., <137 IU/mL) as assessed by COBAS® AmpliPrep/COBAS® TaqMan® CMV test at Week 8 (2 consecutive samples ≥ 5 days apart).[1]

†CMV infection symptom control was defined as resolution or improvement of tissue-invasive disease or CMV syndrome for symptomatic patients at baseline, or no new symptoms for patients who were asymptomatic at baseline.[2]

‡Cochran-Mantel-Haenszel weighted average approach was used for the adjusted difference in proportion (maribavir – IAT), the corresponding 95% CI, and the p-value after adjusting for the transplant type and baseline plasma CMV DNA concentration. Only those with both stratification factors were included in the computation.[1]

Adapted from Avery RK, *et al* 2022.[2]

CI = confidence interval; **CMV** = cytomegalovirus; **HSCT** = haematopoietic stem cell transplant; **IAT** = investigator-assigned therapy (e.g., one or a combination of ganciclovir, valganciclovir, foscarnet, or cidofovir); **SOT** = solid organ transplant.

DYSGEUSIA WAS THE MOST FREQUENTLY REPORTED TEAE WITH LIVTENCITY, RARELY LEADING TO TREATMENT DISCONTINUATION[3,4]

SOLSTICE TRIAL: Adverse events (all grades) reported in >10% of patients receiving LIVTENCITY, ganciclovir/valganciclovir or foscarnet[2]

Adverse event	LIVTENCITY (n=234), %	Ganciclovir/valganciclovir (n=56), %	Foscarnet (n=47), %
Any TEAE	**97**	91	92
Dysgeusia	**37**	4	0
Nausea	**21**	14	30
Diarrhoea	**19**	23	19
Vomiting	**14**	13	17
Anaemia	**12**	7	19
Fatigue	**12**	13	6
CMV[a] viraemia	**10**	7	2
Pyrexia	**10**	11	19
Neutropenia	**9**	34	15
Acute kidney injury	**9**	2	21
Headache	**8**	11	17
Peripheral oedema	**7**	5	11
Hypomagnesemia	**4**	4	15
Hypertension	**4**	2	13
Hypokalaemia	**3**	2	19
Leukopenia	**3**	13	2

[a]Events such as worsening of CMV viraemia were coded to the preferred term of CMV viraemia.[2]

Adapted from Avery RK, *et al* 2022.[2]

SOLSTICE TRIAL: TEAEs leading to treatment discontinuation in ≥2 patients in either treatment group (safety population)[3,4*]

Adverse event	LIVTENCITY (n=234)	IAT (n=116)	Ganciclovir/ Valganciclovir (n=56)	Foscarnet (n=47)
Any TEAE leading to discontinuation	**31** (13.2%)	37 (31.9%)	18 (32.1%)	17 (36.2%)
Any treatment-related TEAE leading to discontinuation[†]	**11** (4.7%)	27 (23.3%)	15 (26.8%)	11 (23.4%)
CMV infection	**7** (3.0%)	1 (0.9%)	0 (0%)	0 (0%)
CMV viraemia	**4** (1.7%)	2 (1.7%)	2 (3.6%)	0 (0%)
Diarrhoea	**2** (0.9%)	1 (0.9%)	1 (1.8%)	0 (0%)
Nausea	**2** (0.9%)	1 (0.9%)	0 (0%)	1 (2.1%)
CMV infection reactivation	**2** (0.9%)	0 (0%)	0 (0%)	0 (0%)
Encephalitis CMV	**2** (0.9%)	1 (0.9%)	0 (0%)	1 (2.1%)
Recurrent acute lymphocytic leukaemia	**2** (0.9%)	0 (0%)	0 (0%)	0 (0%)
Dysgeusia	**2** (0.9%)	0 (0%)	0 (0%)	0 (0%)

*Data for patients who received cidofovir (n=6) and 1 investigator-assigned therapy (n=7) are not presented due to low patient numbers. TEAEs were defined as any adverse event occurring during the on-treatment observation phase. The on-treatment observation phase was from the time of study-assigned treatment initiation through 7 days after the last dose of study-assigned treatment (21 days for cidofovir), or until the LIVTENCITY rescue treatment initiation or the non-study CMV treatment initiation, whichever was earlier. [†]In 2 patients in either treatment group (safety population).

Adapted from Avery RK, *et al* 2022[3] and Alexander BD, *et al* 2022.[4]

AE = adverse event; **CMV** = cytomegalovirus; **IAT** = investigator-assigned therapy (e.g., one or a combination of ganciclovir, valganciclovir, foscarnet, or cidofovir); **TEAE** = treatment-emergent adverse event.

CONTRAINDICATIONS AND DRUG-DRUG INTERACTIONS[1]

CONTRAINDICATIONS[1]

- LIVTENCITY may antagonise the antiviral effect of ganciclovir or valganciclovir. Co-administration with ganciclovir or valganciclovir is contraindicated
- Known hypersensitivity to maribavir or any components of the formulation
  - Magnesium stearate
  - Microcrystalline cellulose
  - Sodium starch glycolate
  - Brilliant blue FCF aluminium lake
  - Macrogol (polyethylene glycol)
  - Polyvinyl alcohol
  - Purified talc
  - Titanium dioxide
- Please refer to the LIVTENCITY current approved Product Information for further details.

USE WITH IMMUNOSUPPRESSANTS[1]

- LIVTENCITY has the potential to increase the concentrations of immunosuppressants that are cytochrome P450 (CYP)3A/P-gp substrates with narrow therapeutic margins (including tacrolimus, cyclosporine, sirolimus and everolimus)
- The plasma levels of these immunosuppressants must be frequently monitored throughout treatment with LIVTENCITY, especially following initiation and after discontinuation of LIVTENCITY, and doses should be adjusted as needed
- Please refer to the LIVTENCITY current approved Product Information for further details.

DRUG-DRUG INTERACTIONS[1]

- LIVTENCITY is primarily metabolised by CYP3A, and medicinal products that induce or inhibit CYP3A are expected to affect the clearance of LIVTENCITY
- The concomitant use of LIVTENCITY and certain medicinal products may result in known or potentially significant medicinal product interactions, some of which may lead to:
  - Possible clinically significant adverse reactions from greater exposure of concomitant medicinal products
  - Reduced therapeutic effect of LIVTENCITY
- Monitoring of patients being concomitantly treated with the following medicinal products by therapeutic area should be performed (please refer to the LIVTENCITY current approved Product Information for further details on the effect of other medicinal products on LIVTENCITY, and the effect of LIVTENCITY on other medicinal products):
  - Acid reducing agents
  - Anti-arrhythmics
  - Antibiotics
  - Anti-convulsants
  - Anti-inflammatories
  - Anti-fungals
  - Anti-hypertensives
  - Anti-mycobacterials
  - Anti-tussives
  - CNS stimulants
  - Herbal products
  - HMG-CoA reductase inhibitors
  - Immunosuppressants
  - Oral anticoagulants
  - Oral contraceptives
  - Sedatives

FOR THE FULL LIST OF CONTRAINDICATIONS AND DRUG-DRUG INTERACTIONS, PLEASE CONSULT THE CURRENT APPROVED LIVTENCITY PRODUCT INFORMATION.

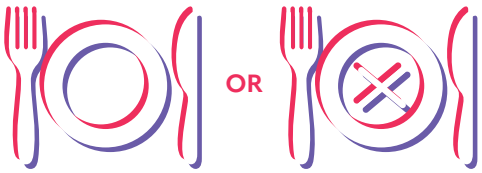
DOSING AND ADMINISTRATION

TWICE-DAILY ORAL ADMINISTRATION

The recommended dose of LIVTENCITY 400 mg (two 200 mg film-coated tablets) twice daily, resulting in a dose 800 mg for 8 weeks[1]

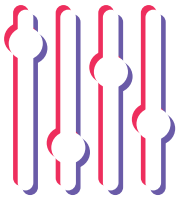
INDIVIDUALISED TREATMENT DURATION

The 8-week treatment duration may need to be individualised based on the clinical characteristics of each patient[1]



CAN BE TAKEN WITH OR WITHOUT FOOD

LIVTENCITY film-coated tablet can be taken as whole, dispersed, or crushed tablets by mouth, or as dispersed tablets through a polyvinyl chloride (PVC) or polyurethane nasogastric or orogastric tube (French size 10 or larger)[1]



NO DOSE ADJUSTMENTS

LIVTENCITY does not require dose adjustments for renal impairment, mild or moderate hepatic impairment, or patients over 65 years[1]

Dose adjustments may be required when LIVTENCITY is co-administered with other medicinal products. Please consult the approved LIVTENCITY Product Information for further information[1]

LIVTENCITY should be initiated by a physician experienced in the management of CMV patients who have undergone SOT or HSCT[1]

CMV = cytomegalovirus; **HSCT** = haematopoietic stem cell transplant; **SOT** = solid organ transplant.

LIVTENCITY®
(maribavir) tablets 200mg

PBS Information: This product is listed on the PBS as a Section 100 item.
Authority required (Streamlined). Refer to PBS Schedule for full authority information.

Please review full Product Information before prescribing.
Product Information is available from Takeda Pharmaceuticals Australia Pty Ltd.
Phone: 1800 012 612. Email: medinfoAPAC@takeda.com

▼ This medicinal product is subject to additional monitoring in Australia. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse events at www.tga.gov.au/reporting-problems.

SCAN HERE TO ACCESS THE FULL PRODUCT INFORMATION

References: 1. LIVTENCITY® Approved Product Information. **2.** Avery RK, *et al. Clin Infect Dis.* 2022;75(4):690-701. **3.** Avery RK, *et al. Clin Infect Dis* 2022;75(4):690-701. (Supplementary data). **4.** Alexander BD, *et al*. Poster 467. Presented at the Transplantation & Cellular Therapy Meetings of ASTCT and CIBMTR. April 23–26, 2022. Salt Lake City, UT.

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ABN 71 095 610 870. C-APROM/AU/LIV/0024. Date of Preparation: June 2025. 2008341.

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