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TEMPLATE: Case Record Form for Visceral Leishmaniasis

Annotated Case Record Form (aCRF) for use in clinical trials in patients with

Visceral Leishmaniasis (VL)

Version 1.0, February 2021

**INSTRUCTION & CONTENTS PAGE**

This Case Record Form template is intended as a guide and may be tailored to collect the data required by the clinical research protocol to answer the specific research question being addressed. It is intended for participants who meet the enrolment criteria as specified in inclusion/exclusion criteria of the study protocol; Clinical Data Acquisition Standards Harmonization (CDASH) annotations are included in blue; Standard Data Tabulation Module (SDTM) in red. Trial sites can select which modules to include in their CRF based on protocol requirements; modules included in the following CRF are below:

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|  | **DATA MODULE** |
| **DAY -7 to DAY /VISIT1**  | Eligibility assessment and randomisation |
| Current episode and previous treatment for VL |
| HIV testing |
| Demographics |
| Past medical history  |
| Medical history (includes signs and symptoms and concomitant acute illness) |
| Previous medication |
| **VISIT 1 & FOLLOW-UP DAYS[[1]](#footnote-1)** | Clinical examination and vital signs |
|  | Laboratory results, including pregnancy |
|  | Parasitological examination |
|  | Study drug administration |
|  | Rescue medication |
|  | Adverse events, serious adverse events and medically attended adverse events  |
|  | Healthcare encounter |
|  | Concomitant medications |
| **DISPOSITION**  | Efficacy assessment (includes clinical and parasitological response)  |
| OR Reason for non-completion of study |
| **APPENDICES**  | 1. Detailed pregnancy assessment
 |
| 1. Electro-cardiogram recording
 |
| 1. Audiometric examination
 |
| 1. Pharmacokinetic sampling
 |
| 1. Radiology testing
 |
| 1. Biomarker testing
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| **SCREENING VISIT (Day -7 to Day 1)** |
| **Date informed consent givenDSDECOD=INFORMED CONSENT** | |\_\_|\_\_|-|\_\_|\_\_|\_\_|-|\_\_|\_\_|\_\_|\_\_| **[DD-MMM-YYYY]** |
| **Date of screeningVISDAT** | |\_\_|\_\_|-|\_\_|\_\_|\_\_|-|\_\_|\_\_|\_\_|\_\_| **[DD-MMM-YYYY]** |
| ELIGIBILITY ASSESSMENT **[IE]** |
| Inclusion CriteriaIETEST (IECAT= INCLUSION)  | **Criterion Description[Adapt as per protocol]** | **Yes** | **No** |
| **IEORRES** |
| INCL001 | Patients for whom written informed consent has been obtained (if aged 18 years and over) or signed by parents(s) or legal guardian for patients under 18 years of age. In the case of minors, assent from the children also needs to be obtained as per each country regulatory requirements. | **€** | **€** |
| INCL002 | Patients with clinical signs and symptoms of VL and confirmatory parasitological microscopic diagnosis or equivalent, as defined in the protocol. | **€** | **€** |
| Exclusion Criteria **IETEST (IECAT=EXCLUSION)** | **Criterion Description****[Adapt as per protocol]** | **Yes** | **No** |
| **IEORRES** |
| EXCL001 | Women of child-bearing potential who are not using an assured method of contraception or are unwilling to use an assured method of contraception for the duration of treatment and (xx) months after as defined in the protocol. | **€** | **€** |
| EXCL002 | Breast-feeding women. | **€** | **€** |
| EXCL003 | Pregnant women. | **€** | **€** |
| EXCL004 | Patients with severe illness as defined in the protocol. | **€** | **€** |
| EXCL005 | Patients who have received any anti-leishmanial drugs in the last [xx] months as defined in the protocol. | **€** | **€** |
| EXCL006 | Patients with previous history of hypersensitivity reaction or known drug class allergy to any of the study treatments. | **€** | **€** |
| EXCL007 | HIV infected patients  | **€** | **€** |
| **Assessment of eligibility at VISIT 1** | **Yes** | **No** |
| **Did the subject meet all eligibility criteria? IEYN** | **€** | **€** |
| RANDOMISATION |
| If applicable, to which group is participant randomised? **ARM ARMCD** |  |

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| CURRENT EPISODE & PREVIOUS TREATMENT FOR VL |
| **Type of VL at presentation** | € Primary | € Relapse | **Has the subject been previously diagnosed with VL?**  | € Yes | € No |
| **If yes, number of previous treatments?** |  | Are previous treatment regimens known? | € Yes | € No |
| *To be considered part of medical history and prior concomitant medications; details of previous VL diagnosis to be included in the MH domain and details of previous treatments for VL to be included in the CM domain* |

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| PREGNANCY TESTING[[2]](#footnote-2) **LBCAT=PREGNANCY *Only applicable to women of child-bearing potential*** |
| **Was a sample taken for pregnancy testing?** **LBPREFYN**  | **€** Yes  | **€** No  | **€** NA[[3]](#footnote-3) | **Date of sample collection** | **|\_\_|\_\_|-|\_\_|\_\_|\_\_|-|\_\_|\_\_|\_\_|\_\_| [DD-MMM-YYYY] LBDAT LBDTC** |
| **Pregnancy test name****LBTEST** | **Not done****LBSTAT** | **Reason not done****LBREASND** | **Result LBORRES** |
|  | **€** | € Pre-menarche€ Permanently sterile[[4]](#footnote-4)€ Postmenopausal€ Refused test€ Other, specify below | € Negative | € Positive |
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| HIV TESTING **[MB]**  |
| **Was a sample taken for HIV testing?** **MBYN [[5]](#footnote-5) where MBTESTCD=HIV** | **€** Yes  | **€** No  |
| **Date of HIV test****MBDAT MBDTC** | **HIV test name****MBTEST** | **Results MBORRES** | **Not done****MBSTAT** | **Reason not done****MBREASND** |
| |\_\_|\_\_|-|\_\_|\_\_|\_\_|-|\_\_|\_\_|\_\_|\_\_| **[DD-MMM-YYYY]** |  | € Positive | € Negative | €  |  |
| |\_\_|\_\_|-|\_\_|\_\_|\_\_|-|\_\_|\_\_|\_\_|\_\_| **[DD-MMM-YYYY]** |  | € Positive | € Negative | €  |  |
| |\_\_|\_\_|-|\_\_|\_\_|\_\_|-|\_\_|\_\_|\_\_|\_\_| **[DD-MMM-YYYY]** |  | € Positive | € Negative | €  |  |

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| DEMOGRAPHICS **[DM]** |
| **Date of completion** | |\_\_|\_\_|-|\_\_|\_\_|\_\_|-|\_\_|\_\_|\_\_|\_\_|[DD-MMM-YYYY] VISDAT | Time of completion | |\_\_|\_\_|:|\_\_|\_\_|[HH:MM] VISTIM |
| **What is the subject’s date of birth?[[6]](#footnote-6)[[7]](#footnote-7)BRTHDAT BRTHDTC** | |\_\_|\_\_|-|\_\_|\_\_|\_\_|-|\_\_|\_\_|\_\_|\_\_| |
| **OR, if BRTHDAT unknown,** **what is the subject’s age?[[8]](#footnote-8)** | |\_\_|\_\_|\_\_|**AGE** | € Weeks | € Months | € Years |
| AGEU |
| **What is the sex of the subject?****SEX** | **€** Male | **€** Female |  |
| **What is the race of the subject****[[9]](#footnote-9)?****CRACE[[10]](#footnote-10) RACE** | **€** Black **€** White**€** Indian **€** Asian**€** Other |
| **If other, specify** **RACEOTH** |  |
| **What is the ethnicity of the subject? ETHNIC** | **€** Eastern Africa**€** South Asia **€** Latin America **€** Unknown **€** Other (specify below) |
| **If other, specify** **ETHNICOTH** |  |

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| HEALTH CARE ENCOUNTER **[HO]**  |
| *If healthcare encounters occurred record each encounter on a separate row* |
| **Were there any healthcare encounters? HOYN** | **€** Yes  | **€** No  |
| **Healthcare encounter** **Number HOSPID** | **Type of healthcare encounter HOCAT** | **Start date HOSTDAT HOSTDTC** | **End date HOSTDAT HOSTDTC** | **Main diagnosis/condition/symptom HOTERM** |
|  | **€** Out-patient**€** In-patient | |\_\_|\_\_|-|\_\_|\_\_|\_\_|-|\_\_|\_\_|\_\_|\_\_| **[DD-MMM-YYYY]** | |\_\_|\_\_|-|\_\_|\_\_|\_\_|-|\_\_|\_\_|\_\_|\_\_| **[DD-MMM-YYYY]** |  |
|  | **€** Out-patient**€** In-patient | |\_\_|\_\_|-|\_\_|\_\_|\_\_|-|\_\_|\_\_|\_\_|\_\_| **[DD-MMM-YYYY]** | |\_\_|\_\_|-|\_\_|\_\_|\_\_|-|\_\_|\_\_|\_\_|\_\_| **[DD-MMM-YYYY]** |  |
|  | **€** Out-patient**€** In-patient | |\_\_|\_\_|-|\_\_|\_\_|\_\_|-|\_\_|\_\_|\_\_|\_\_| **[DD-MMM-YYYY]** | |\_\_|\_\_|-|\_\_|\_\_|\_\_|-|\_\_|\_\_|\_\_|\_\_| **[DD-MMM-YYYY]** |  |
|  | **€** Out-patient**€** In-patient | |\_\_|\_\_|-|\_\_|\_\_|\_\_|-|\_\_|\_\_|\_\_|\_\_| **[DD-MMM-YYYY]** | |\_\_|\_\_|-|\_\_|\_\_|\_\_|-|\_\_|\_\_|\_\_|\_\_| **[DD-MMM-YYYY]** |  |

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| PAST MEDICAL HISTORY**MHCAT=General** |
| **Does the patient have any clinically significant past medical or surgical history?** **MHYN[[11]](#footnote-11)** If yes, record below | **€** Yes | **€** No |
| **What is the term for the past medical history/surgical procedure?****MHTERM** | **Estimated start date[[12]](#footnote-12) MHSTDAT MHSTDTC** | **Estimated end date MHENDAT MHENDTC** | **Or ongoing?[[13]](#footnote-13) MHONGO MHENRTPT/MHENRF** | **Toxicity Grade[[14]](#footnote-14)** **MHTOXGR** |
|  | |\_\_|\_\_|-|\_\_|\_\_|\_\_|-|\_\_|\_\_|\_\_|\_\_|**[DD-MMM-YYYY]** | |\_\_|\_\_|-|\_\_|\_\_|\_\_|-|\_\_|\_\_|\_\_|\_\_|**[DD-MMM-YYYY]** | **€** | **€** Mild | **€** Moderate | **€** Severe |
|  | |\_\_|\_\_|-|\_\_|\_\_|\_\_|-|\_\_|\_\_|\_\_|\_\_|**[DD-MMM-YYYY]** | |\_\_|\_\_|-|\_\_|\_\_|\_\_|-|\_\_|\_\_|\_\_|\_\_|**[DD-MMM-YYYY]** | **€** | **€** Mild | **€** Moderate | **€** Severe |
|  | |\_\_|\_\_|-|\_\_|\_\_|\_\_|-|\_\_|\_\_|\_\_|\_\_|**[DD-MMM-YYYY]** | |\_\_|\_\_|-|\_\_|\_\_|\_\_|-|\_\_|\_\_|\_\_|\_\_|**[DD-MMM-YYYY]** | **€** | **€** Mild | **€** Moderate | **€** Severe |
|  | |\_\_|\_\_|-|\_\_|\_\_|\_\_|-|\_\_|\_\_|\_\_|\_\_|**[DD-MMM-YYYY]** | |\_\_|\_\_|-|\_\_|\_\_|\_\_|-|\_\_|\_\_|\_\_|\_\_|**[DD-MMM-YYYY]** | **€** | **€** Mild | **€** Moderate | **€** Severe |
|  | |\_\_|\_\_|-|\_\_|\_\_|\_\_|-|\_\_|\_\_|\_\_|\_\_|**[DD-MMM-YYYY]** | |\_\_|\_\_|-|\_\_|\_\_|\_\_|-|\_\_|\_\_|\_\_|\_\_|**[DD-MMM-YYYY]** | **€** | **€** Mild | **€** Moderate | **€** Severe |
|  | |\_\_|\_\_|-|\_\_|\_\_|\_\_|-|\_\_|\_\_|\_\_|\_\_|**[DD-MMM-YYYY]** | |\_\_|\_\_|-|\_\_|\_\_|\_\_|-|\_\_|\_\_|\_\_|\_\_|**[DD-MMM-YYYY]** | **€** | **€** Mild | **€** Moderate | **€** Severe |
| VL SYMPTONS ON MEDICAL HISTORY[[15]](#footnote-15) **MHCAT=General** |
| **Did the subject have any of the following signs or symptoms within the last (xx) days? MHYN The variable EVLINT is used to represent “within the last “xx” days”** | € Yes | € No |
| **Symptom MHTERM** | **Yes** | **No** | **If yes, give duration; if ongoing give number of days/weeks since start of symptom** | **Or ongoing**  | **Severity/intensity**  |
| **MHOCCUR** | **MHDUR** | **MHDURU** |  **MHONGO Where MHENRTPT = VISIT1** | **MHSEV** |
| Fever | **€** | **€** |  | **€** Days  | **€** Weeks | **€** Months | **€** | **€** Mild | **€** Moderate | **€** Severe |
| Weight Loss | **€** | **€** |  | **€** Days  | **€** Weeks | **€** Months | **€** | **€** Mild | **€** Moderate | **€** Severe |
| Abdominal pain/discomfort | **€** | **€** |  | **€** Days  | **€** Weeks | **€** Months | **€** | **€** Mild | **€** Moderate | **€** Severe |
| Jaundice | **€** | **€** |  | **€** Days  | **€** Weeks | **€** Months | **€** | **€** Mild | **€** Moderate | **€** Severe |
| Oedema | **€** | **€** |  | **€** Days  | **€** Weeks | **€** Months | **€** | **€** Mild | **€** Moderate | **€** Severe |
| Epistaxis | **€** | **€** |  | **€** Days  | **€** Weeks | **€** Months | **€** | **€** Mild | **€** Moderate | **€** Severe |
| Other bleeding signs | **€** | **€** |  | **€** Days  | **€** Weeks | **€** Months | **€** | **€** Mild | **€** Moderate | **€** Severe |
| Other symptoms | **€** | **€** |  | **€** Days  | **€** Weeks | **€** Months | **€** | **€** Mild | **€** Moderate | **€** Severe |
| If other, specify |  |

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| C0-MORBID CONDITIONS |
| **Has the subject experienced any concomitant illness prior to screening?** **MHYN** | € Yes | € No |
| **What is the term for the condition?****MHTERM** | **Yes** | **No** | **If yes, give duration; if ongoing give number of days/weeks since start of illness** | **Or ongoing?****MHONGO MHENRTPT/MHENRF** |
| **MHOCCUR** | **MHTERMDUR** | **MHDURU** |
| Malaria | **€** | **€** |  | **€** Days  | **€** Weeks  | **€** Months  | **€** |
| Tuberculosis | **€** | **€** |  | **€** Days  | **€** Weeks  | **€** Months  | **€** |
| HIV | **€** | **€** |  | **€** Days  | **€** Weeks  | **€** Months  | **€** |
| Other illness, specify\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ | **€** | **€** |  | **€** Days  | **€** Weeks  | **€** Months  | **€** |
| Other illness, specify\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ | **€** | **€** |  | **€** Days  | **€** Weeks  | **€** Months  | **€** |
| PREVIOUS MEDICATION |
| **Were any medications taken within the last** **(xx) days**[[16]](#footnote-16)? The variable EVLINT is used to represent “within the last “xx” days”CMYN30 | € Yes | € No |
| ***If yes, record on the concomitant medications page (record full trade or generic names)*** |

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| CLINICAL EXAMINATION **VS** |
| **Date examination taken VSDAT**  | |\_\_|\_\_|-|\_\_|\_\_|\_\_|-|\_\_|\_\_|\_\_|\_\_| **[DD-MMM-YYYY]** |
| **Clinical examination measurements VSTEST** | **Results VSORRES** | **Method of measurement/ Units VSORRESU** |
| Weight **WEIGHT\_VSTEST** | |\_\_|\_\_|\_\_|.|\_\_| **WEIGHT\_VSORRES** | kg **WEIGHT\_VSORRESU** |
| Weight-for-age z-score[[17]](#footnote-17) | |\_\_|.|\_\_| **WAZ\_VSORRES** | **€** WHOgrowth standards **VSMETHOD** |
| Height **HEIGHT\_VSTEST** | |\_\_|\_\_|\_\_|.|\_\_| **HEIGHT\_VSORRES** | cm **HEIGHT\_VSORRESU** |
| Height-for-age z-score | |\_\_|.|\_\_| **HAZ\_VSORRES** | **€** WHOgrowth standards **VSMETHOD** |
| MUAC **MUAC\_VSTEST** | |\_\_|\_\_||\_\_| **MUAC\_VSORRES** | mm **MUAC\_VSORRESU** |
| BMI **BMI\_VSTEST** | |\_\_|\_\_|.|\_\_| **BMI\_VSORRES** | kg/m2 **BMI\_VSORRESU** |
| Malnutrition[[18]](#footnote-18) | **€** Yes  | **€** No | **€** z score <-2 (ref. WHOgrowth standards) |
| Severe malnutrition | **€ Y**es  | **€** No | **€** z score <-3 (ref. WHOgrowth standards) |
| Temperature **TEMP\_VSTEST**  | |\_\_|\_\_|.|\_\_|**TEMP\_VSORRES** | **€** °C **€** °FUnits **TEMP\_VSORRESU** | Method **VSMETHOD** | **€** Oral **€** Tympanic |
| Systolic blood pressure **SYSBP\_VSTEST** | **Result VSORRES** | **Position** **VSPOS** | **Units VSORRESU** |
| **|\_\_|\_\_|\_\_|** **SYSBP\_VSORRES** | **€** Supine | **€** Standing | **€** Sitting | mmHg **SYSBP\_VSORRESU** |
| Diastolic blood pressure **DIABP\_VSTEST** | **|\_\_|\_\_|\_\_| DIABP\_VSORRES** | **€** Supine | **€** Standing | **€** Sitting | mmHg **DIABP\_VSORRESU** |
| Pulse **PULSE\_VSTEST** | **|\_\_|\_\_|\_\_| PULSE\_VSORRES** | **€** Supine | **€** Standing | **€** Sitting | beats/minute **PULSE\_VSORRESU** |
| Respiratory rate **RESP\_VSTEST** | **|\_\_|\_\_| RESP\_VSORRES** | **€** Supine | **€** Standing | **€** Sitting | breaths/minute **RESP\_VSORRESU** |

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| **Examination MOLOC** | **Result MOORRES** |  | **Method MOMETHOD** |
| Spleen Size **SPLEEN\_MOTEST=SIZE where MOLOC=SPLEEN** | **|\_\_|\_\_|.|\_\_|****SPLEEN\_MOORRES** | **cm SPLEEN\_MOORRESU** | **€** Ultra-sound **SPLEEN\_MOMETHOD** | **€** Manual palpation  | **€** Other method, if yes specify below**SPLEEN\_MOMETHODOTH** |
|  |
| Liver Size **LIVER\_MOTEST=SIZE where MOLOC=SPLEEN** | **|\_\_|\_\_|.|\_\_|****LIVER\_MOORRES** | **cm LIVER\_MOORRESU** | **€** Ultra-sound **LIVER\_MOMETHOD** | **€** Manual palpation  | **€** Other method, if yes specify below**LIVER\_MOMETHODOTH** |
|  |
| Lymphadenopathy present **PEOCCUR where PETEST = LYMPHNODE ASSESSMENT** | If yes, give location **PELOC** |  | Other, specify **SPECOTH\_LYMPHNODE\_PELOC** |
| **€ Y**es  | **€** No | **€** Axillary**AXILLARY LYMPHNODE\_PELOC** | **€** Cervical**CERVICAL LYMPHNODE\_PELOC** | **€** Inguinal**INGUINAL LYMPHNODE\_TUPEC** | **€** Other**OTHER\_LYMPHNODE\_PELOC** |  |
| If lymphadenopathy present give location | **€** Left**€** Right **€** Bilateral **AXILLARY LYMPHNODE\_PELAT** | **€** Left**€** Right **€** Bilateral **CERVICAL LYMPHNODE\_PELAT** | **€** Left**€** Right **€** Bilateral **INGUINAL LYMPHNODE\_PELAT** |  | **€** Left**€** Right **€** Bilateral **OTHER\_LYMPHNODE\_PELAT** |

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| **Other significant systemic findings such as HEENT, cardiovascular, respiratory, abdominal, skin, musculoskeletal? If yes specify below** | **€ Y**es  | **€** No |
| **What is the term for the medical history condition/event? MHTERM** | **Start date[[19]](#footnote-19)** **MHSTDAT MHSTDTC** | **End date** **MHENDAT MHENDTC** | **Is the medical condition/event ongoing? MHONGO****MHENRTPT** |
|  | |\_\_|\_\_|-|\_\_|\_\_|\_\_|-|\_\_|\_\_|\_\_|\_\_| **[DD-MMM-YYYY]** | |\_\_|\_\_|-|\_\_|\_\_|\_\_|-|\_\_|\_\_|\_\_|\_\_| **[DD-MMM-YYYY]** | **€** |
|  | |\_\_|\_\_|-|\_\_|\_\_|\_\_|-|\_\_|\_\_|\_\_|\_\_| **[DD-MMM-YYYY]** | |\_\_|\_\_|-|\_\_|\_\_|\_\_|-|\_\_|\_\_|\_\_|\_\_| **[DD-MMM-YYYY]** | **€** |
|  | |\_\_|\_\_|-|\_\_|\_\_|\_\_|-|\_\_|\_\_|\_\_|\_\_| **[DD-MMM-YYYY]** | |\_\_|\_\_|-|\_\_|\_\_|\_\_|-|\_\_|\_\_|\_\_|\_\_| **[DD-MMM-YYYY]** | **€** |
|  | |\_\_|\_\_|-|\_\_|\_\_|\_\_|-|\_\_|\_\_|\_\_|\_\_| **[DD-MMM-YYYY]** | |\_\_|\_\_|-|\_\_|\_\_|\_\_|-|\_\_|\_\_|\_\_|\_\_| **[DD-MMM-YYYY]** | **€** |
| **Para-kala-azar dermal leishmaniasis assessment** |
| Does the patient have para-kala-azar dermal leishmaniasis at baseline? | **€ Y**es  | **€** No | If yes, indicate the PKDL severity/grade[[20]](#footnote-20) | **€** Mild[[21]](#footnote-21) | **€** Moderate[[22]](#footnote-22) | **€** Severe[[23]](#footnote-23) |

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| LABORATORY RESULTS[[24]](#footnote-24) |
| **HEMATOLOGY LBCAT=HEMATOLOGY SPEC TYPE = BLOOD** |
| **Were haematology samples** **taken LBPERFYN**  | **€** Yes **€** No  | **Date of sample collection** | **Time of sample collection** |
| |\_\_|\_\_|-|\_\_|\_\_|\_\_|-|\_\_|\_\_|\_\_|\_\_| **[DD-MMM-YYYY]** **LBDAT LBDTC**  | |\_\_|\_\_|:|\_\_|\_\_| **[HH:MM**] **LBTIM LBDTC**  |
| **Haematology test name****LBTEST** | **Results****LBORRES** | **Units[[25]](#footnote-25)****LBORRESU** | **Was the result interpreted as clinically significant[[26]](#footnote-26) LBCLSIG** | **Test done** **LBSTAT**  | **If no, provide reason****LBREASND** |
| Hemoglobin | **|\_\_|\_\_|.|\_\_| HGB\_LBORRES** | Hb (g/dL) **HGB\_LBORRESU** | **€** Yes | **€** No  | **€** Yes | **€** No  |  |
| White cell count | **|\_\_|\_\_|\_\_|.|\_\_|WBC\_LBORRES** | WBC (109/L)**WBC\_LBORRESU** | **€** Yes | **€** No  | **€** Yes | **€** No |  |
| Neutrophils | **|\_\_|\_\_|.|\_\_| NEUT\_LBORRES** | Neutrophils (109/L)**NEUT\_LBORRESU** | **€** Yes | **€** No  | **€** Yes | **€** No |  |
| Basophils | **|\_\_|\_\_|.|\_\_| BASO\_LBORRES** | Basophils (109/L)**BASO\_LBORRESU** | **€** Yes | **€** No  | **€** Yes | **€** No |  |
| Lymphocytes | **|\_\_|\_\_|.|\_\_| LYM\_LBORRES** | Lymphocytes (109/L)**LYM\_LBORRESU** | **€** Yes | **€** No  | **€** Yes  | **€** No |  |
| Monocytes | **|\_\_|\_\_|.|\_\_| MONO\_LBORRES** | Monocytes (109/L)**MONO\_LBORRESU** | **€** Yes | **€** No  | **€** Yes  | **€** No  |  |
| Eosinophils | **|\_\_|\_\_|.|\_\_| EOS\_LBORRES** | Eosinophils (109/L)**EOS\_LBORRESU** | **€** Yes | **€** No  | **€** Yes  | **€** No  |  |
| Platelets | **|\_\_|\_\_|\_\_|\_\_|PLAT\_LBORRES** | Platelets (109/L)**PLAT\_LBORRESU** | **€** Yes | **€** No  | **€** Yes  | **€** No |  |
| Prothrombin time | **|\_\_||\_\_| PT\_LBORRES** | Prothrombin time (seconds)**PT\_LBORRESU** | **€** Yes  | **€** No | **€** Yes  | **€** No |  |
| International-normalised-ratio (INR) | **|\_\_|.|\_\_| INR\_LBORRES** |  | **€** Yes  | **€** No | **€** Yes  | **€** No |  |

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| **BIOCHEMISTRY[[27]](#footnote-27) LBCAT=BIOCHEMISTRY**  |
| **Were biochemistry samples taken? LBPERFYN**  |  **€** Yes | **€** No | **Date of sample collection**  | **Time of sample collection**  |
| |\_\_|\_\_|-|\_\_|\_\_|\_\_|-|\_\_|\_\_|\_\_|\_\_| **[DD-MMM-YYYY]** **LBDAT LBDTC**  | |\_\_|\_\_|:|\_\_|\_\_| **[HH:MM]** **LBTIM LBDTC**  |
| **Biochemistry test name****LBTEST** | **Results****LBORRES** | **Units[[28]](#footnote-28)****LBORRESU** | **Was the result interpreted as clinically significant[[29]](#footnote-29) LBCLSIG** | **Test done** **LBSTAT**  | **If no, provide reason****LBREASND** |
| AST | **|\_\_|\_\_|\_\_|\_\_|****AST\_LBORRES** | AST (IU/L)**AST\_LBORRESU** | **€** Yes  | **€** No | **€** Yes  | **€** No |  |
| ALT | **|\_\_|\_\_|\_\_|\_\_|****ALT\_LBORRES** | ALT (IU/L)**ALT\_LBORRESU** | **€** Yes  | **€** No | **€** Yes  | **€** No |  |
| Total Bilirubin | **|\_\_|\_\_|\_\_|.|\_\_|****BILI\_LBORRES** | Total bilirubin (µmol/L ) **BILI\_ORRESU** | **€** Yes  | **€** No | **€** Yes  | **€** No |  |
| Creatinine | **|\_\_|\_\_|\_\_|\_\_|** **CREAT\_LBORRES** | Creatinine (µmol/L) **CREAT\_LBORRESU** | **€** Yes  | **€** No | **€** Yes  | **€** No |  |
| Albumin | **|\_\_|\_\_|\_\_|** **ALB\_LBORRES** | Albumin (g/L) **MG\_LBORRESU** | **€** Yes  | **€** No | **€** Yes  | **€** No |  |
| Fasting Blood Glucose**LBTEST = Blood glucose and LBFAST = Y** | **|\_\_|\_\_|\_\_|** **GLU\_LBORRES** | Glucose (mmol/L) **GLU\_LBORRESU** | **€** Yes  | **€** No | **€** Yes  | **€** No |  |

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| **URINALYSIS LBCAT=URINALYSIS SPEC TYPE = URINE** |
| **Was a sample taken for urinalysis? LBPERFYN [[30]](#footnote-30)** | **€** Yes **€** No  | **Date and time of sample collection** | |\_\_|\_\_|-|\_\_|\_\_|\_\_|-|\_\_|\_\_|\_\_|\_\_| **[DD-MMM-YYYY] LBDAT LBDTC** |
| |\_\_|\_\_|:|\_\_|\_\_**|** **[HH:MM]** **LBTIM LBDTC** |
| **Urinalysis test name****LBTEST** | **Method****LBMETH** | **Results****LBORRES** | **If abnormal, clinically relevant LBCLGIG** |
| Blood | **€** Dipstix | **€** Negative  | € 1+  | € 2+  | € 3+ | € 4+  | **€** Yes  | **€** No |
| Protein | **€** Dipstix | **€** Negative  | € 1+  | € 2+  | € 3+ | € 4+  | **€** Yes  | **€** No |
| Glucose | **€** Dipstix | **€** Negative  | € 1+  | € 2+  | € 3+ | € 4+  | **€** Yes  | **€** No |
| Bilirubinuria | **€** Dipstix | **€** Negative  | € 1+  | € 2+  | € 3+ | € 4+  | **€** Yes  | **€** No |
| Ph | **€** Dipstix | **|\_\_|.|\_\_| PH\_LBORRES** | **€** Yes  | **€** No |

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| PREGNANCY TESTING[[31]](#footnote-31) **LBCAT=PREGNANCY *Only applicable to women of child-bearing potential*** |
| **Was a sample taken for pregnancy testing?** **LBPREFYN**  | **€** Yes  | **€** No  | **€** NA[[32]](#footnote-32) | **Date of sample collection** | **|\_\_|\_\_|-|\_\_|\_\_|\_\_|-|\_\_|\_\_|\_\_|\_\_| [DD-MMM-YYYY] LBDAT LBDTC** |
| **Pregnancy test name****LBTEST** | **Not done****LBSTAT** | **Reason not done****LBREASND** | **Result LBORRES** |
|  | **€** | € Pre-menarche€ Permanently sterile[[33]](#footnote-33)€ Postmenopausal€ Refused test€ Other, specify below | € Negative | € Positive |
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| VISCERAL LEISCHMANIASIS DIAGNOSTIC **MB where MBTEST=LEISCHMANIA** |
| **Was a VL RDT[[34]](#footnote-34) performed?** **MBPERFYN** | **€** Yes | **€** No | **If not done, give reason MBREASND**  |  | **If yes, date test performed****MBDAT MBDTC** | |\_\_|\_\_|-|\_\_|\_\_|\_\_|-|\_\_|\_\_|\_\_|\_\_|**[DD-MMM-YYYY]** |
| **Test type****MBTEST** | **€** rK39  | **€** Other | Other, specify **MBMETHODOTH**  |  | **Result MBORRES** | **€** Positive  | **€** Negative  |
| **Was a Direct Agglutination Test (DAT) performed?** **MBPERFYN** | **€** Yes | **€** No | **If not done, give reason MBREASND**  |  | **If yes, date test performed****MBDAT MBDTC** | |\_\_|\_\_|-|\_\_|\_\_|\_\_|-|\_\_|\_\_|\_\_|\_\_|**[DD-MMM-YYYY]** |
| **Test type****MBTEST**  | **€** DAT  | **€** Other | Other, specify **MBMETHODOTH**  |  | **Result MBORRES** | **€** Positive  | **€** Negative | **€** Intermediate |

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| PARASITOLOGICAL EXAMINATION [**MB] where MBMETHOD= VISCERAL LEISCHMANIASIS MICROSCOPY and MBTEST = LEISCHMANIA** |
| **Was parasitological examination performed****? MBPERFYN** |  **€** Yes **€** No | **If not done, reason not done MBREASND** |  |
| **Date sample collected****MBDAT MBDTC** | **Time sample collected****MBTIM MBDTC**  | **Site of Aspirate****MBLOC** | **Result of Aspirate MBTSTDTL**  | **Grading of parasite count[[35]](#footnote-35) MBORRES** |
| |\_\_|\_\_|-|\_\_|\_\_|\_\_|-|\_\_|\_\_|\_\_|\_\_|**[DD-MMM-YYYY]** | |\_\_|\_\_|:|\_\_|\_\_|**[HH:MM]**  | **€** Spleen **€** Bone marrow**€** Lymph Node  | **€** Positive | **€** 6+  | **€** 5+ | **€** 4+ |
| **€** 3+ | **€** 2+  | **€** 1+  |
| **€** Negative | **€** 0  |

*Once all investigations have been completed the eligibility criteria page will be completed; if the participant is eligible for the study as detailed in the study protocol, the randomisation module will be completed, and treatment phase will be started.*

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| **TREATMENT PHASE (DAY1)** |
| STUDY DRUG ADMINISTRATION[[36]](#footnote-36) [[37]](#footnote-37) [**EC]** |

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| **DRUG SENSITIVITY TESTING** *Complete if patient receives Amphotericin B IV* |
| **Was drug sensitivity testing done?** | **€** Yes  | **€** No  | **If yes, dose given** |  | **Units** | **€** Mg  | **Result** | **€** Reaction |
| **€** No reaction |

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| *Please complete a separate CRF page for each study drug administered* |
| **ORAL MEDICATION** |
| **Was oral medication given** **ECDOSROUTE = ORAL** | **If yes name of drug ECTRT** | **Prescribed daily amount ECDOSPCB** | **Dose units****ECDOSU** | **Weight used to calculate dose at Day 1** | **Frequency of dose administration[[38]](#footnote-38) ECDOSFRQ** |
| **€** Yes  | **€** No  |  |  | **€ mg/day** | |\_\_|\_\_|.|\_\_|kg | **€** QD | **€** BID | **€** TID | **€** QID |
| **EXAMPLE OF AN ORAL DOSE SCHEDULE GIVEN TWICE DAILY** |
| **Date dose administered****ECSTDAT ECSTDTC****Time dose administered****ECSTTIM ECSTDTC** | **OR****Missed dose ECOCCUR**  | **Reason for missed dose****ECSTAT** | **Dose formulation ECDOSFRM** | **Number of tablets/****capsules given** **ECDOSNUM** | **Dose amount/capsule or tablet (mg) ECDOSAMT** | **Did the subject vomit within (xx) minutes of the dose FAORRES where FAOBJ = VOMITING, FACAT = POST-DOSE VOMITING; When vomiting occurs, an AE record is created where AEPRESP=Y and AETERM=VOMITING** | **Time of vomit****AESTDAT****AESTDTC** | **Dose/Re-treatment****RDIND****SUPPEC.QVAL** |
| |\_\_|\_\_|-|\_\_|\_\_|\_\_|-|\_\_|\_\_|\_\_|\_\_|**[DD-MMM-YYYY]**|\_\_|\_\_|:|\_\_|\_\_| **[HH:MM]** | € |  | € Tablet€ Capsule |  | |\_\_||\_\_||\_\_| | € Yes  | € No  | |\_\_|\_\_|:|\_\_|\_\_| **[HH:MM]** | € Dose € Re-dose  |
| |\_\_|\_\_|-|\_\_|\_\_|\_\_|-|\_\_|\_\_|\_\_|\_\_|**[DD-MMM-YYYY]**|\_\_|\_\_|:|\_\_|\_\_| **[HH:MM]** | € |  | € Tablet€ Capsule |  | |\_\_||\_\_||\_\_| | € Yes  | € No  | |\_\_|\_\_|:|\_\_|\_\_| **[HH:MM]** | € Dose € Re-dose  |
| |\_\_|\_\_|-|\_\_|\_\_|\_\_|-|\_\_|\_\_|\_\_|\_\_|**[DD-MMM-YYYY]**|\_\_|\_\_|:|\_\_|\_\_| **[HH:MM]** | € |  | € Tablet€ Capsule |  | |\_\_||\_\_||\_\_| | € Yes  | € No  | |\_\_|\_\_|:|\_\_|\_\_| **[HH:MM]** | € Dose € Re-dose  |
| |\_\_|\_\_|-|\_\_|\_\_|\_\_|-|\_\_|\_\_|\_\_|\_\_|**[DD-MMM-YYYY]**|\_\_|\_\_|:|\_\_|\_\_| **[HH:MM]** | € |  | € Tablet€ Capsule |  | |\_\_||\_\_||\_\_| | € Yes  | € No  | |\_\_|\_\_|:|\_\_|\_\_| **[HH:MM]** | € Dose € Re-dose  |

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| **INTRAVENOUS/INTRAMUSCULAR INJECTION** |
| *Please complete a separate CRF page for each study drug administered* |
| **Was intravenous or intramuscular treatment given** **If, yes ECDOSFRM=INJECTION** | **If yes, give name of drug ECTRT** | **Dose units****ECDOSU** | **Weight used to calculate dose at Day 1[[39]](#footnote-39)** | **Frequency of dose administration[[40]](#footnote-40) ECDOSFRQ** | **Route of administration[[41]](#footnote-41) ECDOSROUTE** |
| **€** Yes  | **€** No  |  | € mg | € mg/kg | |\_\_|\_\_|.|\_\_|kg | **€** QD  | **€** BID | **€** IV | **€** IM |
| **EXAMPLE OF AN INTRAVENOUS/MUSCULAR DOSE SCHEDULE GIVEN DAILY** |
| **Date of dose ECSTDAT ECSTDTC****Time of dose ECSTTIM ECSTDTC** | **Dose amount prescribed ECDOSPCB** | **Dose amount given ECDOSADM** | **Was study treatment interrupted[[42]](#footnote-42) ECDOSINT** | **If yes, give reason****ECDOSCHRS** | **Was treatment permanently discontinued ECDOSDC** | **If treatment permanently discontinues, give reason ECDOSDC** | **If other, specify** |
| |\_\_|\_\_|-|\_\_|\_\_|\_\_|-|\_\_|\_\_|\_\_|\_\_|**[DD-MMM-YYYY]**|\_\_|\_\_|:|\_\_|\_\_| **[HH:MM]** | **|\_\_||\_\_||\_\_||\_\_|** | **|\_\_||\_\_||\_\_||\_\_|** | **€** Changed **DOSCH** **€** Interrupted **DOSITR** |  | **€** Yes **€** No  | **€** Adverse event **€** Other  |  |
| |\_\_|\_\_|-|\_\_|\_\_|\_\_|-|\_\_|\_\_|\_\_|\_\_|**[DD-MMM-YYYY]**|\_\_|\_\_|:|\_\_|\_\_| **[HH:MM]** | **|\_\_||\_\_||\_\_||\_\_|** | **|\_\_||\_\_||\_\_||\_\_|** | **€** Changed **DOSCH** **€** Interrupted **DOSITR** |  | **€** Yes **€** No  | **€** Adverse event **€** Other  |  |
| |\_\_|\_\_|-|\_\_|\_\_|\_\_|-|\_\_|\_\_|\_\_|\_\_|**[DD-MMM-YYYY]**|\_\_|\_\_|:|\_\_|\_\_| **[HH:MM]** | **|\_\_||\_\_||\_\_||\_\_|** | **|\_\_||\_\_||\_\_||\_\_|** | **€** Changed **DOSCH** **€** Interrupted **DOSITR** |  | **€** Yes **€** No  | **€** Adverse event **€** Other  |  |

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| **FOLLOW-UP ASSESSMENTS VISIT DAY2 etc** |
| **Was the visit completed? VISYN**  | **€** Yes | **€** No |
| **Date of visit VISDAT VISDTC** | **OR reason not completed** |
| |\_\_|\_\_|-|\_\_|\_\_|\_\_|-|\_\_|\_\_|\_\_|\_\_|**[DD-MMM-YYYY]** | **€** Withdrew consent**€** Withdrawn due to adverse event**€** Withdrawn due to treatment failure**€** Lost to follow-up**€** Death**€** Other, specify \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ |

*Repeat data modules/case report forms relevant to protocol EG. Signs & symptoms of VL, physical examination, laboratory tests, pregnancy test, ECG, audiometry, and/or parasitological tests.*

*Note: Adverse event monitoring and concomitant medication completion need to be completed at each visit.*

*NB: Most studies will report on initial treatment and clinical outcome at Day28 0r Day30, at this visit the following modules needs to be completed in addition to the modules repeated above:*

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| POST-KALA-AZAR DERMAL LEISHMANIASIS (PKDL) ASSESSMENT |
| **Does the patient have signs /symptoms of dermal leishmaniasis at this visit[[43]](#footnote-43)?** | **€** Yes | **€** No |
| **If the patient did not have PKDL at baseline, has it developed?** | **€** Yes | **€** No | **€** NA**[[44]](#footnote-44)** |
| **If the patient had PKDL at baseline, has it worsened[[45]](#footnote-45)?** | **€** Yes | **€** No | **€** NA |
| **If yes for either PKDL questions, give date PKDL developed (if not present at baseline), OR date PKDL worsened (present at baseline)** | |\_\_|\_\_|-|\_\_|\_\_|\_\_|-|\_\_|\_\_|\_\_|\_\_|**[DD-MMM-YYYY]** |
| *The grading of PKDL is currently being completed for the Africa regions where VL is endemic (such as Sudan), refer to the VL data standard user guide for more information* |
| **If relevant, severity of PKDL[[46]](#footnote-46)** | **€** Mild[[47]](#footnote-47) | **€** Moderate[[48]](#footnote-48) | **€** Severe[[49]](#footnote-49) |

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| VL SYMPTONS at FOLLLOW-UP ASSESSMENTS: CLINICAL EVENTS **[CE]** |
| **Did the subject have any of the following signs or symptoms since the last visit? CEYN The variable EVLINT is used to represent “since the last visit”** | € Yes | € No | **Date of clinical assessment CEDAT CEDTC** | |\_\_|\_\_|-|\_\_|\_\_|\_\_|-|\_\_|\_\_|\_\_|\_\_|**[DD-MMM-YYYY]** |
| **Symptom CETERM** | **Yes** | **No** | **If yes, give duration; if ongoing give number of days/weeks since start of symptom** | **Or ongoing[[50]](#footnote-50)**  | **Severity/intensity**  |
| **CEOCCUR** | **CEDUR** | **CEDURU** |  **CEONGO CEENRTPT** | **CESEV** |
| Fever | **€** | **€** |  | **€** Days  | **€** Weeks | **€** Months | **€** | **€** Mild | **€** Moderate | **€** Severe |
| Weight Loss | **€** | **€** |  | **€** Days  | **€** Weeks | **€** Months | **€** | **€** Mild | **€** Moderate | **€** Severe |
| Abdominal pain/discomfort | **€** | **€** |  | **€** Days  | **€** Weeks | **€** Months | **€** | **€** Mild | **€** Moderate | **€** Severe |
| Jaundice | **€** | **€** |  | **€** Days  | **€** Weeks | **€** Months | **€** | **€** Mild | **€** Moderate | **€** Severe |
| Oedema | **€** | **€** |  | **€** Days  | **€** Weeks | **€** Months | **€** | **€** Mild | **€** Moderate | **€** Severe |
| Epistaxis | **€** | **€** |  | **€** Days  | **€** Weeks | **€** Months | **€** | **€** Mild | **€** Moderate | **€** Severe |
| Other bleeding signs | **€** | **€** |  | **€** Days  | **€** Weeks | **€** Months | **€** | **€** Mild | **€** Moderate | **€** Severe |
| Other symptoms | **€** | **€** |  | **€** Days  | **€** Weeks | **€** Months | **€** | **€** Mild | **€** Moderate | **€** Severe |
| If other, specify |  |

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| FEVER CLEARANCE **VS**  | VISIT DAY 28 |
| *Fever clearance time will be calculated from date and time of onset of treatment to date and time of the last fever peak, after which there was a period of at least 72 hours with no fever. Record below the details of the last fever peak after which there was a period of at least 72 hours with no fever, or as specified in the protocol* |
| **Date temperature measured VSDAT LBDTC** | **Time temperature measured VSTIM LBDTC** | **Temperature TEMP\_VSORRES** | **Units of measure VSORRESU** | **Method of measurement VSMETHOD** |
| |\_\_|\_\_|-|\_\_|\_\_|\_\_|-|\_\_|\_\_|\_\_|\_\_| **[DD-MMM-YYYY]** | |\_\_|\_\_|:|\_\_|\_\_| **[HH:MM]**  | |\_\_|\_\_|.|\_\_| | **€** °C **€** °F | **€** Oral**€** Tympanic |

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| RESCUE MEDICATION[[51]](#footnote-51) |
| **Was rescue medication given?** | **Reason for initiation of rescue treatment** | **If other, specify** |
| **€** Yes  | **€** No | **€** Adverse event  | **€** Initial failure(DXX) | **€** Relapse | **€** PKDL  | **€** Other |  |
| *If yes, complete details on concomitant medications page* |

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| ADVERSE EVENTS **[AE]** *(make multiple copies of this page if necessary)* |
| **Any AEs? AEYN [[52]](#footnote-52)** | **€** Yes | **€** No | **What is the AE term? AETERM** |  | **AE number AESPID** |  |
| **Start date/time** | **|\_\_|\_\_|-|\_\_|\_\_|\_\_|-|\_\_|\_\_|\_\_|\_\_| [DD-MMM-YYYY]****AESTDAT AESTDTC** | **End date/time** | **|\_\_|\_\_|-|\_\_|\_\_|\_\_|-|\_\_|\_\_|\_\_|\_\_|****[DD-MMM-YYYY] AEENDAT AEENDTC** | **Ongoing? AEONGO** **MHENRTPT/MHENRF** |
| **|\_\_|\_\_|:|\_\_|\_\_| [HH:MM]****AESTTIM AESTDTC** | **|\_\_|\_\_|:|\_\_|\_\_| [HH:MM]****AEENTIM AEENDTC** | **€** |
| **Standard toxicity grade[[53]](#footnote-53)****AETOXGRV** | **€** Grade 1**AETOXGRV4\_1** | **€** Grade 2**AETOXGRV4\_2** | **€** Grade 3**AETOXGRV4\_3** | **€** Grade 4**AETOXGRV4\_3** | **€** Grade 5**AETOXGRV4\_3** |  |
| **Outcome****AEOUT** | **€** Recovered/ Resolved | **€** Recovered/ Resolved with  sequelae | **€** Recovering/ Resolving | **€** Not recovered/ Not resolved | **€** Fatal | **€** Unknown |
| **Relationship to study treatment AEREL** | **€** Not related | **€** Probably not  related | **€** Possibly related | **€** Probably related | **€** Definitely related |
| **Action taken with study treatment AEACN** | **€** Dose increased | **€** Dose reduced | **€** Dose not changed | **€** Drug interrupted | **€** Drug withdrawn | **€** Not applicable | **€** Unknown |
| **Is the AE serious[[54]](#footnote-54)****AESER** | **Is this a special interest AE? AESI** | **Was a concomitant or additional treatment given due to this adverse event? AECONTRT** | **Was the AE detected at a medically attended visit[[55]](#footnote-55)?** **MAAE** |
| **€** Yes | **€** No | **€** Yes | **€** No | **€** Yes | **€** No | **€** Yes | **€** No |
| **Give short description of the AE** |  |

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| SERIOUS ADVERSE EVENTS – REPEAT AS REQUIRED |
| **What is the AE number** | **AE number AESPID** |  |
| **SAE Classification** | **€** Fatal[[56]](#footnote-56) **AESDTH****€** Life threatening **AESLIFE****€** Requires or prolongs hospitalization **AESHOSP****€** Results in permanent or significant disability/incapacity **AESDISAB****€** Congenital anomaly/birth defect **AESCONG****€** Medically significant **AESMIE**Describe medically significant condition: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ | **If hospitalization/ prolonged hospitalization give admission date****HOSTDAT where HOTERM = HOSPITALIZATION** | |\_\_|\_\_|-|\_\_|\_\_|\_\_|-|\_\_|\_\_|\_\_|\_\_|**[DD-MMM-YYYY]** |
| **If hospitalization/prolonged hospitalization give discharge date****HOENDAT where HOTERM = HOSPITALIZATION** | |\_\_|\_\_|-|\_\_|\_\_|\_\_|-|\_\_|\_\_|\_\_|\_\_|**[DD-MMM-YYYY]** |
| **Give short description of the SAE** |  |

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| PRIOR & CONCOMITANT MEDICATION [[57]](#footnote-57) [**CM]** |
| **Was any medication given? CMYN** [[58]](#footnote-58) | **€** Yes[[59]](#footnote-59)  | **€** No |
| **Medication name****CMTRT** | **Category of treatment****CMCAT** | **Frequency[[60]](#footnote-60)****CMDOSFREQ** | **Dose formulation****CMDOSFRM** | **Dose amount****CMDOSAMT** | **Units CMDOSU** | **Route of administration[[61]](#footnote-61)CMROUTE** | **Start date CMSTDAT CMSTDTC****Start time CMTIM CMSTDTC** | **End date CMENDAT CMENDTC****End time CMENTIM CMENDTC** | **Indication****CMINDC** |
|  | **€** Prior**€** During**€** Rescue | **€** QD**€** BID**€** TID**€** QID | **€** tablet**€** susp.**€** injection |  | **€** mL**€** mg | **€** PO**€** TOP**€** SC**€** IM**€** IV**€** PR  | |\_\_|\_\_|-|\_\_|\_\_|\_\_|-|\_\_|\_\_|\_\_|\_\_|**[DD-MMM-YYYY]** | |\_\_|\_\_|-|\_\_|\_\_|\_\_|-|\_\_|\_\_|\_\_|\_\_|**[DD-MMM-YYYY]** |  |
| |\_\_|\_\_|:|\_\_|\_\_| **[HH:MM]** | |\_\_|\_\_|:|\_\_|\_\_| **[HH:MM]** |
|  | **Ongoing? CMONGO CMENRTPT/CMENRF** | **€**  |
|  | **€** Prior**€** During**€** Rescue | **€** QD**€** BID**€** TID**€** QID | **€** tablet**€** susp.**€** injection |  | **€** mL**€** mg | **€** PO**€** TOP**€** SC**€** IM**€** IV**€** PR  | |\_\_|\_\_|-|\_\_|\_\_|\_\_|-|\_\_|\_\_|\_\_|\_\_|**[DD-MMM-YYYY]** | |\_\_|\_\_|-|\_\_|\_\_|\_\_|-|\_\_|\_\_|\_\_|\_\_|**[DD-MMM-YYYY]** |  |
| |\_\_|\_\_|:|\_\_|\_\_| **[HH:MM]** | |\_\_|\_\_|:|\_\_|\_\_| **[HH:MM]** |  |
|  | **Ongoing? CMONGO CMENRTPT/CMENRF** | **€**  |  |

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| INITIAL OUTCOME AT DAY 28 |
| **€** Initial cure[[62]](#footnote-62) | Clinical improvement, defined as improvement of clinical signs and symptoms (absence of fever attributed to VL, reduction in spleen size and improvement of haematological parameters); absence of parasites in the spleen or bone marrow microscopy, and no rescue therapy on or before Day 28 |
| **€** Initial failure | Presence of parasites in spleen or bone marrow on microscopy, requiring rescue therapy on or before Day 28 |

*This section will be used for clinical guidance only, this section will not be for* submission

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| SUBJECT DISPOSITION **[DS] DSCAT = DISPOSITION EVENT** |
| **Did the subject complete the study and all follow-up visits? DSTERM** | **€ Yes**  | **€ No** |
| **[DSDECOD]** | **€** Completed  |
| **If no, list reason for non-completion [DSDECOD]** | **€** Adverse event |
|  | **€** Disease relapse |
|  | **€** Initial failure |
|  | **€** Lost to follow-up |
|  | **€** Non-compliance with study drug |
|  | **€** Death |
|  | **€** Physician decision. Give reason: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ |
|  | **€** Withdrawal by parent/guardian |
|  | **€** Withdrawal by subject |
|  | **€** Protocol major deviation |
| **What was the date of the final assessment**[[63]](#footnote-63) **DSSTDAT DSSTDTC** | **|\_\_|\_\_|-|\_\_|\_\_|\_\_|-|\_\_|\_\_|\_\_|\_\_| [DD-MMM-YYYY]** |

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| OVERALL RESPONSE TO TREATMENT **[RS] where RSTEST=OVERALL RESPONSE** |
| *This section will be completed for all patients in the trial at their last study visit, this might not be the final protocol defined study visit EG, Day 180 such as instances where a patient died or was considered lost-to-follow-up.* |
| **€** | **Final Cure –** absence of signs and symptoms of VL at last study visit (EG. Day 180), and no rescue treatment at any time during the study **RSORRES\_CURE** |
| **€** | **Failure – Initial Failure**: presence of parasites in spleen or bone marrow on microscopy, requiring rescue therapy at or before day 28 **RSORRES\_PARASITIOLOGICAL FAILURE** |
| **€** | **Failure – Relapse**: Initial cure at Day 28, but presented with clinical signs and symptoms of VL with confirmed presence of parasites in spleen or bone marrow on microscopy after day 28 **RSORRES\_RELAPSE** |
| **€** | **Failure** – Treatment discontinuation due to (S)AE related to the study drug, requiring rescue therapy **RSORRES\_TREATMENT\_DISCONTINUED** |
| **€** | **Failure -** Death associated with VL or related to the study drug **RSORRES\_DEATH** |
| **€** | **Other –** Non-completion due to withdrawal, death not related to VL, lost to follow up, protocol violation etc. **RSORRES\_TREATMENT\_DISCONTINUES** |
| Comment |  |

# APPENDICES

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| APPENDIX A |
| DETAILED PREGNANCY ASSESSMENT **[RP]** |
| **Is the subject pregnant?****RPTEST=Pregnant During the Study****RPTESTCD=PREGST** | **€** Yes | **€** No | **€** UNK[[64]](#footnote-64) | **€** NA[[65]](#footnote-65) | **If yes, date of last menstrual period (LMP) RPTEST= Last Menstrual Period Start Date****RPTESTCD=LMPSTDTC** | |\_\_|\_\_|-|\_\_|\_\_|\_\_|-|\_\_|\_\_|\_\_|\_\_|**[DD-MMM-YYYY]****RPORRES where RPTEST=Last Menstrual Period Start Date** |
| **RPORRES where RPTEST = Pregnant During the Study** |  |
| **If pregnant, estimate gestational age** **RPTEST=Estimated Gestational Age****RPTESTCD=EGESTAGE** | |\_\_|\_\_| **RPORRES where RPTEST=Estimated Gestational Age** | **Weeks RPORRESU where RPTEST=Estimated Gestational Age** |
| **Gestational age determined by****RPMETHOD where PTESTCD=EGESTAGE** | **If other, specify****RPMETHOTH** |
| **€** Fundal ht[[66]](#footnote-66) | **€** LMP[[67]](#footnote-67)  | **€** Ultrasound | **€** Other |  |

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| APPENDIX B |
| ECG RECORDING **[EG]** | *If the ECG is to be taken more than once at a study time-point (EG. Triple ECG), record ECG number EG ECG1, ECG2 etc. and repeat ECG module for each recording and the final result for analysis* |
| **Was the ECG recorded?****EGYN [[68]](#footnote-68)**  | **€** Yes  | **€** No | **If not done, give reason EGREASND** |  | **Method EGMETHOD** | **€** Standard12 Lead **12-LEAD STANDARD** |
| **Number of ECG****EGSEQ** | **Date ECG recorded EGDAT EGDTC** | **Time ECG recorded****EGTIM EGDTC** |
|  | |\_\_|\_\_|-|\_\_|\_\_|\_\_|-|\_\_|\_\_|\_\_|\_\_|**[DD-MMM-YYYY]** | |\_\_|\_\_|:|\_\_|\_\_|**[HH:MM]** |
| **ECG TEST RESULTS** |
| **ECG test name****EGTEST** | **Results****EGORRES** | **Units[[69]](#footnote-69)****EGORRESU** | **Not done****EGSTAT** | **Reason not done****EGREASND** |
| **RR-interval**  | **|\_\_|\_\_|\_\_|\_\_| RRMEAN\_EGORRES** | MSEC | **€** |  |
| **PR-interval**  | **|\_\_|\_\_|\_\_| PRMEAN\_EGORRES** | MSEC | **€** |  |
| **QT-interval[[70]](#footnote-70)**  | **|\_\_|\_\_|\_\_| QTMEAN\_EGORRES** | MSEC | **€** |  |
| **QRS-duration**  | **|\_\_|\_\_|\_\_| QRSDUR\_EGORRES** | MSEC | **€** |  |

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| **Overall ECG Results EGINTP** | **€** Normal | **€** Abnormal | **If Abnormal, Was the ECG clinically Significant? EGCLSIG** | **€** Yes | **€** No |

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| APPENDIX C |
| AUDIOMETRIC EXAMINATION[[71]](#footnote-71) **[AU]** |  **Was Audiometry performed?****AUYN [[72]](#footnote-72)** | **€ Yes**  | **€ No**  | **€ NA[[73]](#footnote-73)** |
| **Date of Audiometry AUDAT AUDTC** | |\_\_|\_\_|-|\_\_|\_\_|\_\_|-|\_\_|\_\_|\_\_|\_\_|**[DD-MMM-YYYY]** |  |
| **THRESHOLD FREQUENCY[[74]](#footnote-74)** |
| **Frequency (Hz)****AUHZNUM** | **Ear Side****AULOC** | **Results AUORRES** | **Units****[[75]](#footnote-75)****AUORRESU** | **Ear Side****AULOC** | **Results AUORRES** | **Units****AUORRESU** |
| **1000** | LEFT | **|\_\_|\_\_|****125HL\_AUORRES** | dB | RIGHT | **|\_\_|\_\_|****125HR\_AUORRES** | dB |
| **2000** | LEFT | **|\_\_|\_\_|****500HL\_AUORRES** | dB | RIGHT | **|\_\_|\_\_|****500HR\_AUORRES** | dB |
| **3000** | LEFT | **|\_\_|\_\_|****1000HL\_AUGORRES** | dB | RIGHT | **|\_\_|\_\_|****1000HR\_AUORRES** | dB |
| **4000** | LEFT | **|\_\_|\_\_|****2000HL\_AUGORRES** | dB | RIGHT | **|\_\_|\_\_|****2000HR\_AUORRES** | dB |
| **6000** | LEFT | **|\_\_|\_\_|****4000HL\_AUGORRES** | dB | RIGHT | **|\_\_|\_\_|****4000HR\_AUORRES** | dB |
| **8000** | LEFT | **|\_\_|\_\_|****8000HL\_AUORRES** | dB | RIGHT | **|\_\_|\_\_|****8000HR\_AUORRES** | dB |
| **Otoscopic Findings[[76]](#footnote-76) AUINTP** | **Left ear**  |  Normal  |  Abnormal | **Right ear**  |  Normal  |  Abnormal |
| **If abnormal, describe AUSTRESC**  |  |  |

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| **APPENDIX D** |
| **PHARMACOKINETIC SAMPLING** [[77]](#footnote-77)  **[PK]** | **Was PK sampling performed?****PCYN**[[78]](#footnote-78) | **€ Yes**  | **€ No** | **€ NA[[79]](#footnote-79)** |
| **Date and actual time of sample collection** **PCDAT PCDTC** | **Time-point[[80]](#footnote-80)****PCTPT** | **Sample type PCSPEC** | **Sample condition****PCSPCCND** | **Not done****PCSTAT** | **Reason not done****PCREASND** |
| |\_\_|\_\_|-|\_\_|\_\_|\_\_|-|\_\_|\_\_|\_\_|\_\_|**[DD-MMM-YYYY]**|\_\_|\_\_|:|\_\_|\_\_| **[HH:MM]** | **PREDOSE** | **€** Serum**€** Plasma |  | **€**  |  |
| **€** Blood  | **€** Dried |
| |\_\_|\_\_|-|\_\_|\_\_|\_\_|-|\_\_|\_\_|\_\_|\_\_|**[DD-MMM-YYYY]**|\_\_|\_\_|:|\_\_|\_\_| **[HH:MM]** | **D1H6** | **€** Serum**€** Plasma |  | **€**  |  |
| **€** Blood | **€** Dried |
| |\_\_|\_\_|-|\_\_|\_\_|\_\_|-|\_\_|\_\_|\_\_|\_\_|**[DD-MMM-YYYY]**|\_\_|\_\_|:|\_\_|\_\_| **[HH:MM]** | **D7** | **€** Serum**€** Plasma |  | **€**  |  |
| **€** Blood  | **€** Dried |

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| **APPENDIX E** |
| **RADIOLOGY SCREENING [RE]** | **Was Radiology done for this study? REYN** | **€ Yes**  | **€ No** |
| **Radiology type[[81]](#footnote-81) REMETHOD** | **Date of radiograph REDAT** | **Location of radiograph RELOC** | **Result RECLSIG** | **Not done****RESTAT** | **Reason not done****REREASND** |
| **€** Radiograph **€** Ultra-sound**€** POCUS **€** CT scan**€** Other | |\_\_|\_\_|-|\_\_|\_\_|\_\_|-|\_\_|\_\_|\_\_|\_\_|**[DD-MMM-YYYY]** | € Chest € Spleen€ Liver € Other (describe  below) **RELOCOTH** | € Normal € Abnormal NCS (describe below)€ Abnormal CS (describe below) **REORRES** | **€**  |  |
|  |  |
| **€** Radiograph **€** Ultra-sound**€** POCUS **€** CT scan**€** Other | |\_\_|\_\_|-|\_\_|\_\_|\_\_|-|\_\_|\_\_|\_\_|\_\_|**[DD-MMM-YYYY]** | € Chest € Spleen€ Liver € Other (describe below) **RELOCOTH** | € Normal € Abnormal NCS (describe below)€ Abnormal CS (describe below) **REORRES** | **€**  |  |
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| **APPENDIX F** |
| **BIOMARKER [MB]****Where MBTEST = Leishmania** | **Was a sample taken for PCR, qPCR or LAMP? MBYN**[[82]](#footnote-82) | **€ Yes**  | **€ No** |
| **Date of sample collection** **MBDAT MBDTC** | **Test type****MBTEST** | **Sample type MBSPEC** | **Manufacturer****DIVAL when DIPARM=Manufacturer** | **Lot number****DIVAL when DIPARM=Lot** | **Trade name****DIVAL when DIPARM=Trade Name** | **Primers used**  |
| |\_\_|\_\_|-|\_\_|\_\_|\_\_|-|\_\_|\_\_|\_\_|\_\_|**[DD-MMM-YYYY]** | **€** PCR **€** qPCR**€** LAMP | **€** Venous blood**€** Other (describe below)**MBSPREOTH** | **€** Eiken Chemical Co., Japan**€** Other (describe below)**DIVALOTH** |  |  | **€** ITS-1 **€** Other (describe below)  |
|  |  |  |
| **Not done****MBSTAT** | **Reason not done MBREASND** | **Results qualitative MBTSTDTL** | **Results quanitative MBORRES** | **Units of measure****MBORRESU** |
| **€**  |  | **€** Positive  | **€** Negative |  | **€** Parasites/uL of blood**€** Parasites/ug of genomic DNA |

1. Recommended follow-up after treatment is at 3 and 6 months. [↑](#footnote-ref-1)
2. If there is a risk of a change in pregnancy test kit during the study, manufacturer, trade name and lot number (from the DI CDISC domain) need to be included at the individual patient level and recorded on the CRF. [↑](#footnote-ref-2)
3. Males. [↑](#footnote-ref-3)
4. Hysterectomy, bilateral salpingectomy, and bilateral oophorectomy. [↑](#footnote-ref-4)
5. For data management, not for inclusion in SDTM. [↑](#footnote-ref-5)
6. In some countries local privacy law may not allow DOB, in this instance age should be used. [↑](#footnote-ref-6)
7. If actual date is unknown use 99 or 999 for place holder for ANY day and month. [↑](#footnote-ref-7)
8. Only record age if DOB unknown, if child aged less than 5 years record in months, if older than 5 years record in years [↑](#footnote-ref-8)
9. As recommended by FDA, see VL Standard user guide. [↑](#footnote-ref-9)
10. The CDASH variable CRACE (Collected Race) is used in addition to the variable RACE (Race) when more detailed race categorizations are desired (e.g., use of race designations other than those used by the FDA). For additional guidance using this variable please refer to the CDASHIG v2.0 and the SDTMIG v3.2. See controlled terminology for full code-list of race as collected [https://evs.nci.nih.gov/ftp1/CDISC/SDTM/]. [↑](#footnote-ref-10)
11. For data management, not for inclusion in SDTM. [↑](#footnote-ref-11)
12. If the actual date is unknown use 99 or 999 as a place holder for ANY day and month. [↑](#footnote-ref-12)
13. Check if the condition is still present at the baseline visit. [↑](#footnote-ref-13)
14. The grading will be specified in the study protocol. [↑](#footnote-ref-14)
15. Self-reported signs and symptoms of VL at diagnosis. [↑](#footnote-ref-15)
16. Previous medication duration will be specified in the study protocol. [↑](#footnote-ref-16)
17. Some sites might calculate weight-for-age, height-for-age and weight-height-for-age using a standard such as WHO growth curves; these might further be used to classify a nutritional status such as malnutrition and severe malnutrition. [↑](#footnote-ref-17)
18. In these instances, the z score cut-off used for classification of nutritional status will be defined in the protocol. [↑](#footnote-ref-18)
19. If the actual date is unknown use 99 or 999 as a place holder for ANY day and month. [↑](#footnote-ref-19)
20. PKDL grading is currently only used in Africa, mainly Sudan but included here as an example as could be a useful tool for other regions. If grading scales are used these will be defined in the protocol. [↑](#footnote-ref-20)
21. Mild (Grade 1): scattered macular, papular or nodular rash on the face with or without lesions on the upper chest or arms. [↑](#footnote-ref-21)
22. Moderate (Grade 2): dense macular. papular or nodular rash covering most of the face and extending to the chest, back, upper arms and legs; with only scattered lesions on the forearms and legs. [↑](#footnote-ref-22)
23. Severe (Grade 3): dense maculopapular or nodular rash covering most parts of the body, including the hands and feet; the mucosa of the lip and palate may be involved. [↑](#footnote-ref-23)
24. The laboratory tests and units shown above are an example, use the laboratory tests and units specified in the protocol. [↑](#footnote-ref-24)
25. The units of measure are an example, the protocol will specify which unit’s lab. values to be recorded in. [↑](#footnote-ref-25)
26. Clinical significance will be specified in the protocol. [↑](#footnote-ref-26)
27. The laboratory tests and units shown above are an example, use the laboratory tests and units specified in the protocol, others to consider could be alkaline phosphatase and indirect bilirubin. [↑](#footnote-ref-27)
28. The units of measure are an example, the protocol will specify which unit’s laboratory values to be recorded in. [↑](#footnote-ref-28)
29. Clinical significance will be specified in the protocol. [↑](#footnote-ref-29)
30. For data management, not for inclusion in SDTM. [↑](#footnote-ref-30)
31. If there is a risk of a change in pregnancy test kit during the study, manufacturer, trade name and lot number (from the DI CDISC domain) need to be included at the individual patient level and recorded on the CRF. [↑](#footnote-ref-31)
32. Males. [↑](#footnote-ref-32)
33. Hysterectomy, bilateral salpingectomy, and bilateral oophorectomy. [↑](#footnote-ref-33)
34. RDT=rapid diagnostic test. [↑](#footnote-ref-34)
35. 6+ > 100 parasites per field; 5+ 10-100 parasites per field; 4+ 1-10 parasites per field; 3+ 1-10 parasites per 10 fields; 2+ 1-10 parasites per 100 fields; 1+ 1-10 parasites per 1000 fields; 0 = 0 parasite per 1000 fields . Note grading of parasites is only relevant in spleen and bone marrow samples, the definitions of grading need to be included in the metadata. [↑](#footnote-ref-35)
36. Record each dose of study medication given; if a dose is re-administered after initial dose was vomited this will be recorded in a new row in SDTM (see user guide). [↑](#footnote-ref-36)
37. If study drug is interrupted due to rescue treatment, record in concomitant medications module. [↑](#footnote-ref-37)
38. QD=once daily; BID twice daily; TID= three times a day; QID=four times a day. These are suggestions only the frequency of oral dose administration will be specified in the protocol. [↑](#footnote-ref-38)
39. Clinical guide only, not for submission. [↑](#footnote-ref-39)
40. QD=daily; BID= twice daily. These are suggestions only the frequency of oral dose administration will be specified in the protocol. [↑](#footnote-ref-40)
41. IV=intravenous; IM=intramuscular. [↑](#footnote-ref-41)
42. If study treatment is interrupted and restarted, enter details on new row of study treatment. [↑](#footnote-ref-42)
43. This section is for clinical guidance only, if PKDL is detected during the follow-up period or PKDL was present at baseline and has worsened on physical examination, **PETERM = PKDL,** details need to be captured in the AE module. [↑](#footnote-ref-43)
44. Not applicable, PKDL an exclusion criteria. [↑](#footnote-ref-44)
45. Worsened could be mild/moderate at baseline and assessed as moderate/severe at follow-up. [↑](#footnote-ref-45)
46. Some sites might use a severity grading such as the example included, see user guide for additional detail. [↑](#footnote-ref-46)
47. scattered macular, papular or nodular rash on the face with or without lesions on the upper chest or arms. [↑](#footnote-ref-47)
48. dense macular. papular or nodular rash covering most of the face and extending to the chest, back, upper arms and legs; with only scattered lesions on the forearms and legs. [↑](#footnote-ref-48)
49. dense maculopapular or nodular rash covering most parts of the body, including the hands and feet; the mucosa of the lip and palate may be involved. [↑](#footnote-ref-49)
50. Symptom still present at date of assessment, if symptom has resolved at assessment, this field will be blank. [↑](#footnote-ref-50)
51. This section is intended for clinical guidance, not for submission; the study drug treatment will be stopped, and the details of rescue medication will be recorded as **CMCAT=rescue**, see concomitant and prior medications module. [↑](#footnote-ref-51)
52. For data management, not for inclusion in SDTM. [↑](#footnote-ref-52)
53. Toxicity grade according to a standard toxicity scale such as CTCAE (Common Terminology Criteria for Adverse Events). The name of the scale and the version should be mentioned in the metadata. [↑](#footnote-ref-53)
54. If classified as serious, please complete a SAE CRF. [↑](#footnote-ref-54)
55. Visits outside of routine study visits as defined in the protocol. [↑](#footnote-ref-55)
56. If SAE is fatal, date of death will be the same as end date of AE. [↑](#footnote-ref-56)
57. The period for reporting concomitant medications will be specified in the protocol. [↑](#footnote-ref-57)
58. List any prescription/non-prescription/traditional meds, vitamins, herbal/dietary supplements, or vaccinations given, if none were given check No for “Was any medication given?” [↑](#footnote-ref-58)
59. If concomitant medications were given, enter full trade or generic names. [↑](#footnote-ref-59)
60. QD=once daily; BID twice daily; TID= three times a day; QID=four times a day. These are suggestions only, others include QM=every month; PRN=as needed; U=unknown. [↑](#footnote-ref-60)
61. PO=oral; TOP=topical; SC=subcutaneous; IM=intramuscular; IV=intravenous; PR=per rectal. These are suggestions others include transdermal, intraocular, inhalation, intra-lesion, intraperitoneal, nasal, vaginal. [↑](#footnote-ref-61)
62. Based on follow-up discussion from the VL study outcome working group [↑](#footnote-ref-62)
63. This date relates to last contact date in lost-to-follow-up, last study visit. Date of last study visit if withdrawn by participant or investigator, date of death if participant died and last study visit date for other. [↑](#footnote-ref-63)
64. UNK = unknown [↑](#footnote-ref-64)
65. NA = not applicable [↑](#footnote-ref-65)
66. Ht = height [↑](#footnote-ref-66)
67. LMP=Last Menstrual Period [↑](#footnote-ref-67)
68. For data management, not for inclusion in SDTM [↑](#footnote-ref-68)
69. The units of measure are an example, the protocol will specify which unit’s the ECG parameters are to be recorded [↑](#footnote-ref-69)
70. The study protocol may require a calculated adjustment for the QT interval, this will be generated in the analysis, and the corrected result and method of correcting included in the analysis considerations section of the VL standard user guide [↑](#footnote-ref-70)
71. Some studies might use a hearing grading score to determine the severity of hearing loss, this grading category will be specified in the protocol, see VL data standard user guide for additional information [↑](#footnote-ref-71)
72. For data management, not for inclusion in SDTM [↑](#footnote-ref-72)
73. NA = not applicable (not required for this study protocol). [↑](#footnote-ref-73)
74. The specific frequency in Hz will be specified in the protocol and could range from 125 Hz – 8000 Hz, these are examples to be replaced by protocol specified thresholds. [↑](#footnote-ref-74)
75. The units of measure are an example, the protocol will specify which unit’s the hearing parameters are to be recorded in. [↑](#footnote-ref-75)
76. Some sites may will use a grading to determine level of hearing in each ear, such as grading table included. [↑](#footnote-ref-76)
77. The analyte name, drug concentration results and units of measure will be a direct upload as an excel/csv file from the pharmacology laboratory responsible for these assays [↑](#footnote-ref-77)
78. For data management, not for inclusion in SDTM [↑](#footnote-ref-78)
79. NA = not applicable (not required for this study protocol) [↑](#footnote-ref-79)
80. The specific time-points will be documented in the protocol [↑](#footnote-ref-80)
81. If more than one radiology procedure done, list each on a separate row on CRF [↑](#footnote-ref-81)
82. For data management, not for inclusion in SDTM [↑](#footnote-ref-82)