**Appendix 1: Inclusion and Exclusion Criteria:**

 **SCREENING INCLUSION CRITERIA**

**Participants must fulfil all of the following inclusion criteria to be eligible for participation in the study:**

* Age 18-75 years at the time of the screening visit
* Able to provide informed consent and comply with study procedures
* Sporadic ALS diagnosed as probable, laboratory-supported probable or definite according to the World Federation of Neurology El Escorial revised criteria as determined by a neurologist with neuromuscular subspecialty training
* Diagnosis <24 months from date of enrolment
* Vital capacity at least 60% of predicted value for gender, height and age at the screening visit
* If taking riluzole, must be on a stable dose for at least 30 days prior to the screening visit, or stopped taking riluzole at least 30 days prior to the screening visit
* Participant has established care with a neurologist at one up to four specialized ALS clinics involved in the study and will maintain this clinical care throughout the study
* Participants can participate in clinical registries, but will be excluded to this protocol if they are participating in a clinical trial involving additional or investigative treatment exposure.

**SCREENING EXCLUSION CRITERIA**

Participants who meet the following criteria were excluded from the study:

A participant was excluded if he or she has any of the following:

* Dependence on mechanical ventilation at the time of screening
* Gastrostomy at the time of screening
* Absence of Upper Motor Neuron Signs
* Participation in any other investigational drug trial or using investigational drug (within 12 weeks prior to screening)
* Known hypersensitivity to dolutegravir, abacavir or lamivudine, or to any of the excipients
* Presence of the HLA-B\*5701 allele at screening
* Presence of a monogenic cause of ALS (e.g. known mutation in SOD1, expansion in c9orf72 etc.)
* History of positive test or positive result at screening for HIV
* Participants positive for Hepatitis B at screening (+HBsAg), or anticipated need for Hepatitis C virus (HCV) therapy during the study;
* Women must not be able to become pregnant (post-menopausal for >1 year, surgically sterile, adequate contraception) or breastfeed for the duration of the study. Women of childbearing potential must have a negative pregnancy test at screening and be non-lactating
* Other interventional clinical trial
* Participant is taking medication contraindicated with Triumeq. Dofetilide (or pilsicainide [available in Japan]) is prohibited as DTG may inhibit its renal tubular secretion resulting in increased dofetilide concentrations and potential for toxicity.
* Presence of any of the following clinical conditions at the time of screening: o Drug or alcohol abuse o Unstable medical disease (such as unstable angina or chronic obstructive pulmonary disease), or active infectious disease (such as Hepatitis B or C or tuberculosis), or current malignancy o Unstable psychiatric illness defined as psychosis or untreated major depression within 90 days of the screening visit. This exclusion criteria is based on a prior psychiatric diagnosis that is unstable as determined by the participant’s treating Psychiatrist o Dementia as previously diagnosed by a medical practitioner
* Safety Laboratory Criteria at the screening visit: o Alanine aminotransferase (ALT) ≥5 times the upper limit of normal (ULN), OR ALT ≥3xULN and bilirubin ≥1.5xULN (with >35% direct bilirubin) o Total bilirubin, lactate, triglycerides, amylase, or lipase greater than 2.0 times the upper limit of normal. Participant has creatinine clearance of < 1\*109/L o Platelet concentration of < 100\*109/L o Haemoglobin < 100g/L

**Appendix 2: Schedule of Visits**





**Appendix 3: HERV-K Analysis**

Serum was centrifuged at 300 g for 10 minutes to clear cell debris, and total nucleic acids were extracted from the supernatant (500 ul) with Ultrasens kit (Qiagen, [Hilden, Germany](https://www.google.com/search?rlz=1C1GCEA_enUS769US769&q=Hilden+Germany&stick=H4sIAAAAAAAAAOPgE-LUz9U3sDQ2z7JQAjON401yk7S0spOt9POL0hPzMqsSSzLz81A4VhmpiSmFpYlFJalFxQBsGJzXRAAAAA&sa=X&ved=2ahUKEwiy_deZqczdAhVC4VMKHVisAn8QmxMoATAdegQIChAg)), following manufacturer’s instructions. Samples having less than 500 ul were excluded from the analysis. Nucleic acids were eluted in 30 ul of AVE buffer (RNase-free water with 0.04% Sodium azide). Digital PCR was performed in duplicate in a QX200 AutoDG Droplet Digital PCR System (Bio-Rad, Hercules, CA, USA) with two sets of primers and probes: one (FAM labeled) to detect HERV-K *env* and another (HEX labeled) to detect the genomic copies of the single copy gene RPP30. RPP30 copy number was used as a measure of cellular DNA in the serum sample. The master mix was composed of 8.75 ul of water, 12.5 ul of ddPCR Supermix (no dUTP) (Bio-Rad, Hercules, CA, USA), 1.25 ul of a mix of HERV-K *env* primers (900 nm) and probe (250 nm), 1.25 ul of ddPCR RPP30 copy number assay (20X; assay ID: dHsaCP1000485) (both from Bio-Rad (Hercules, CA, USA)) and 2.5 ul of the extracted nucleic acids. The empty wells of the PCR plate were filled with a mix of 12.5 ul of ddPCR Control Buffer (Bio-Rad, Hercules, CA, USA) and 12.5 ul of water, to get a similar viscosity in all wells. After preparing the droplets, the PCR was performed in a T100 Thermal cycler (Bio-Rad. Hercules, CA, USA) with these cycling conditions: 95oC for 10 minutes, 40 cycles of 95oC for 30 seconds and 60oC for 1 minute, and 95oC for 10 minutes. Finally, the number of copies was determined in the digital PCR reader. The following primer and probe sequences were used to detect HERV-K *env*: forward primer: 5’ ATTTGGTGCCAGGAACTGAG 3’; reverse primer: 5’ GCTGTCTCTTCGGAGCTGTT 3’and probe 5’ 6-FAM-AGGAGTTGCTGATGGCCTCG-Iowa Black FQ 3’. A blast search of the HERV-K *env* primers used in this study on the [Human GRCh38.p12](https://useast.ensembl.org/Homo_sapiens/Info/Index?db=core;r=11:62369216-62370362;tl=j8xrtBCSQ0O3yq0D-4557238-704065003) identified the HERV-K loci detected with 100% homology:

|  |  |  |  |
| --- | --- | --- | --- |
| **Chromosome** | **Start** | **End** | **Amplicon length** |
| 1 |  75382253 |  75382431 | 179 bp |
| 1 |  155627693 |  155627871 | 179 bp |
| 1 |  160698811 |  160698989 | 179 bp |
| 2 |  129962985 |  129963163 | 179 bp |
| 3 |  113025296 |  113025474 | 174 bp |
| 3 |  125898560 |  125898733 | 179 bp |
| 4 |  165001719 |  165001893 | 175 bp |
| 5 |  156658733 |  156658911 | 179 bp |
| 6 |  77717964 |  77718142 | 179 bp |
| 7 |  4591957 |  4592153 | 179 bp |
| 7 |  4583453 |  4583631 | 179 bp |
| 8 |  7498902 |  7499080 | 179 bp |
| 8 | 139460933 | 139461111 | 179 bp |
|  8 KI270813v1 alt | 182005 | 182183 | 179 bp |
| 11 | 118722041 | 118722219 | 179 bp |
| 12 | 58328486 |  58328664 | 179 bp |
| 19 |  27638644 |  27638822 | 179 bp |
| 19 |  35572497 |  35572675 | 179 bp |
| 19 GL383576 v1 alt | 76109 |  76287 | 179 bp |
| 19 GL383575 v2 alt | 11481 |  11659 | 179 bp |
| 22 |  18946647 |  18946825 | 179 bp |