**Supplementary Table 1. Evidence (trials) considered for country appraisals of nusinersen and voretigene neparvovec**Grey = standard process, White = supplemental process

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **NUSINERSEN** | | | | | | | | | | | | | | | | | | | | | |
| **Trial name /other** | **Type** | **Patient population** | | **N** | **Duration (months)** | **BENELUXA** | | **ENGLAND** | | **FRANCE** | **NL** | | **BELGIUM** | **GERMANY** | | **NORWAY** | | **SCOTLAND** | **SWEDEN** | | **U.S.** |
| **ENDEAR†**1 | Phase III | Type 1 | | 121 | 13† | ‡ | | ‡ | | ‡ | ‡ | | ‡ | ‡ | | ‡ | | ‡ | ‡ | | ‡ |
| **CHERISH** | Phase III | Types 2, 3 | | 126 | 15 | ‡ | | ‡ | | ‡ | ‡ | | ‡ | ‡ | | ‡ | | ‡ | ‡ | | ‡ |
| **SHINE**2 | Open label Extension | Types 1-3 | | 292 | 96 |  | | **√** | |  |  | |  |  | |  | | **√** | **√** | | **√** |
| **CS3A** | Open label, dose escalation | Type 1 | | 21 | 45 |  | |  | |  |  | |  |  | |  | |  |  | | **√** |
| **CS2/CS12** | Open label | Types 2, 3 later onset | | 28 | 36 | **√** | | **√** | |  | **√** | | **√** |  | |  | |  | **√** | | **√** |
| **EMBRACE**3 | Phase II | Types 1-3 | | 21 | 34 |  | | **√** | |  |  | |  |  | |  | |  | **√** | | **√** |
| **NURTURE** | Phase II Single arm | Pre-symptomatic | | 20 | On-going | **√** | | **√** | |  | **√** | | **√** |  | | **√** | | **√** | **√** | | **√** |
| **Expanded access programs**4 | Open label cohort | Type 1 | | 3 stud-ies | On-going |  | | **√** | |  |  | |  |  | |  | |  |  | | **√** |
| **VORETIGENE NEPARVOVEC** | | | | | | | | | | | | | | | | | | | | | |
| **Trial name /other** | **Type** | **N** | **FRANCE** | | **NL** | | **U.S.** | | **ENGLAND** | | | **GERMANY** | | | **NORWAY** | | **SCOTLAND** | | | **SWEDEN** | |
| **301**5 | Phase III open label RCT comparing long term efficacy and safety | 21 | ‡ | | ‡ | | ‡ | | ‡ | | | ‡ | | | ‡ | | ‡ | | | ‡ | |
| **302**5 | Extension study | 10 |  | |  | | **√** | | **√** | | | **√** | | | **√** | | **√** | | | **√** | |
| **101/102**6 | Phase I open label, dose escalating safety profile | 12 |  | | **√** | | **√** | | **√** | | |  | | | **√** | | **√** | | | **√** | |

**‡** Primary trial **√** Additional trials considered in appraisal **†** Trial stopped early due to exceptional circumstances: good results  
 1**ENDEAR** is a statistically significant positive interim analyses results caused study to end early based on recommendation of independent data and safety monitoring board.   
2**SHINE** is an open label extension study for people who participated in ENDEAR or CHERISH, to evaluate long term safety and tolerability, and efficacy.  
3**EMBRACE** is for SMA patients not eligible to participate in the clinical studies ENDEAR and CHERISH.   
4**Expanded Access Program (EAP)** isto provide Nusinersen to Patients with Infantile-onset SMA.  
5**Study 301/302:** Study 301 is a RCT comparison of treatment in both eyes to basic standard of care with a 3-4 year follow up. After 1 year, standard of care patients from study 301 could receive treatment in extension study 302.   
6**Study 101/102:** Study 101: 1 injection in 1 eye, Study 102: 1 year later - injection in other eye - 15 year follow up.

*Notes.* For Nusinersen, all countries considered the endpoint 'motor milestone response' in their decision, which was the primary endpoint for both the ENDEAR and CHERISH studies. All countries also considered the main secondary endpoints from the ENDEAR study in their decision, which were 'overall' and 'event free' survival.

For Voretigene, all countries considered the endpoint 'performance on MLMT mobility test' in their decision. Only some countries considered the secondary endpoints 'full field light sensitivity' and 'visual acuity', but this did not depend on whether countries had standard or supplemental processes for RDTs.