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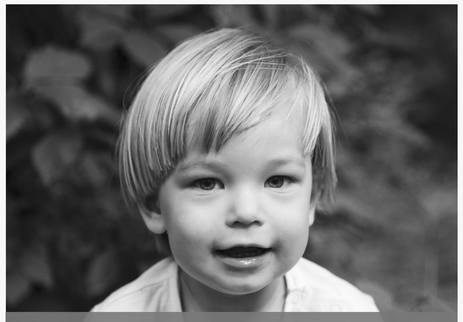
Translarna™ Case Studies:

Demonstrated real-life results in patients with nonsense mutation Duchenne muscular dystrophy (nmDMD)

Because *every* moment counts

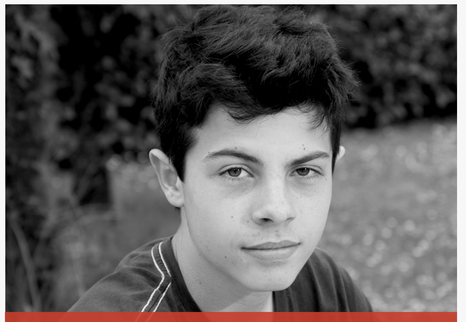


Case 1: Demonstrated efficacy of Translarna in a young patient

Case 2: Importance of starting Translarna early

Case 3: Translarna delayed decline in a severely impaired patient

Case 4: Translarna helped preserve muscle function for longer



Case 5: Importance of continual Translarna treatment

The goal of treatment with Translarna is to slow the progression of nmDMD. Individual treatment results will vary.

Translarna is indicated for the treatment of Duchenne muscular dystrophy resulting from a nonsense mutation in the dystrophin gene, in ambulatory patients aged 2 years and older in the European Member States and Iceland, Liechtenstein, Norway, Great Britain, Northern Ireland, Kazakhstan, Israel, Republic of Korea, Belarus, Russia, Brazil, Peru, Chile, and Macedonia, and aged 5 years and older in the Kingdom of Saudi Arabia and Ukraine (under special state registration). In Brazil, the indication is specific to male paediatric patients. The presence of a nonsense mutation in the dystrophin gene should be determined by genetic testing (Translarna Summary of Product Characteristics (SmPC) for respective countries).

Translarna received a conditional marketing authorisation in the European Member States and Iceland, Liechtenstein, Norway, Great Britain and Northern Ireland.

▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system. Adverse events should also be reported to PTC Therapeutics at pharmacovigilance@ptcbio.com

This information is intended for Healthcare Professionals only.

Translarna™ (ataluren) treatment has demonstrated effectiveness in patients with nmDMD, slowing the progression of their disease[1-6]

Real-world data from the STRIDE Registry* showed that Translarna delayed loss of ambulation in nmDMD patients[2†]

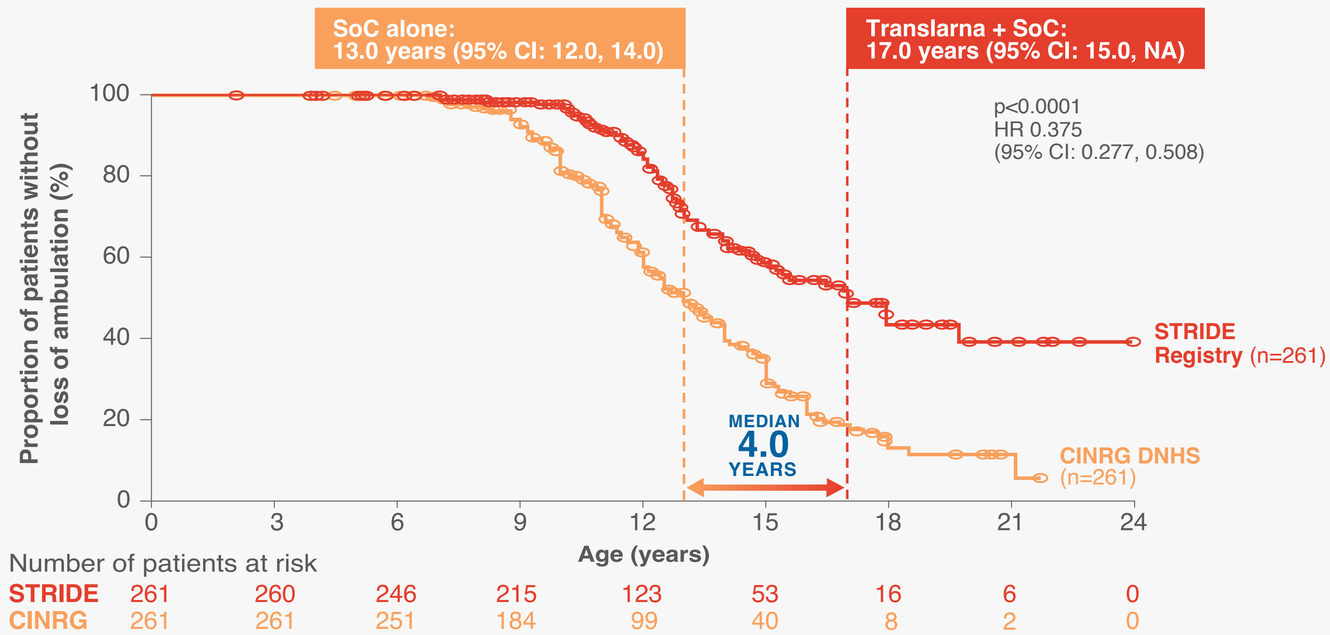
Mercuri E WMS 2022 STRIDE Poster/Col 3/ Fig 3

Delay to loss of ambulation

4.0 YEARS†

Translarna + SoC* provided **4.0 years† of additional ambulation** vs SoC alone* in real-world patients with DMD[2]

MEDIAN AGE AT LOSS OF AMBULATION



Number of patients at risk

STRIDE	261	260	246	215	123	53	16	6	0
CINRG	261	261	251	184	99	40	8	2	0

Real-world data from STRIDE also showed that:

Translarna + SoC preserved physical function for longer vs treatment with SoC alone[3‡]

Translarna could delay pulmonary function decline in nmDMD patients[3§]

Translarna was generally well tolerated by patients in the STRIDE Registry, **with TEAEs in most patients being mild or moderate**[3‖]

Translarna is the first and only approved dystrophin restoration therapy in Europe addressing the underlying cause of nmDMD in ambulatory patients aged 2 years and older.[1]

*As of 31 January, 2022, 261 nmDMD patients from the STRIDE Registry were individually matched with 261 DMD patients from CINRG DNHS using established measures of disease progression (age at first clinical symptoms, age at first corticosteroid use, duration of deflazacort use, duration of other corticosteroid use). An acknowledged limitation of this analysis is that populations were not matched according to mutation type or location. SoC refers to corticosteroids (deflazacort, prednisolone, and prednisone) and palliative therapies.[2] CINRG DNHS is the largest natural history study to date in DMD and represents a real-world control group for comparison with STRIDE. Patients were followed closely for several years: median treatment follow-up was 1796 days.[3,7] †The study assessed the difference in median age at loss of ambulation: 17.0 years (STRIDE) vs 13.0 years (CINRG DNHS), HR 0.375 (95% CI: 0.277, 0.508); p<0.0001.[2] ‡As measured by time to climb 4 stairs and time to stand from supine. Median age at worsening of time to climb 4 stairs to ≥10 seconds: milestone not reached (STRIDE) vs 13.2 years (CINRG DNHS). HR 0.385 (95% CI: 0.172, 0.859); p=0.0195. Median age at worsening of time to stand from supine to ≥10 seconds: STRIDE 14.0 years, CINRG DNHS 9.9 years. HR 0.290 (95% CI: 0.140, 0.642); p=0.0008.[3] §Study authors noted there was a trend toward delayed worsening of pulmonary function, but that due to short duration of follow-up and low number of events, it is premature to draw firm conclusions from these results.[3] ‖The most common TEAEs (in >1% of patients) were gait inability (3.3% [seven patients]), cough, diarrhoea, femur fracture, vomiting (1.9% [4 patients] each), back pain, gastroenteritis, and headache (1.4% [3 patients] each). Twelve patients (5.6%) experienced serious adverse events.[3]

CI, confidence interval; CINRG DNHS, Cooperative International Neuromuscular Research Group Duchenne Natural History Study; DMD, Duchenne muscular dystrophy; HR, hazard ratio; NA, not applicable; nmDMD, nonsense mutation Duchenne muscular dystrophy; SoC, standard of care; STRIDE, Strategic Targeting of Registries and International Database of Excellence; TEAE, treatment-emergent adverse event.

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CASE 1: Demonstrated efficacy of Translarna in a young patient

Translarna led to improved muscle strength and disappearance of Gowers' sign in a 3-year-old boy[8]

INITIAL PRESENTATION

- **Increased creatine kinase** (5941 U/L), **CK-MB** (243 ng/mL), and **myoglobin** (1857 ng/mL) observed at 3 months of age[8]
- **Delay in motor and language milestones** reported by the mother at 21 months of age[8]
  - Neurological exam showed evidence of Gowers' sign
  - North Star Ambulatory Assessment (NSAA) total score was 10/34

DIAGNOSIS

- **Genetic testing** at 3 months of age was consistent with a diagnosis of **nmDMD**[8]
  - Mutation c.10801C > T; p.Gln3601X, exon 76

TREATMENT HISTORY

- 2 years of age: **Translarna initiated** (40 mg/kg/day)[8]
- 2 years, 8 months and 3 years, 4 months: NSAA was administered to evaluate motor function[8]

Early diagnosis and treatment of nmDMD can help to prevent muscle degeneration and improve outcomes[8]

Translarna is the first and only approved dystrophin restoration therapy in Europe addressing the underlying cause of nmDMD in ambulatory patients aged 2 years and older[1]

Translarna preserved physical function for longer in real-world nmDMD patients, enabling them to be more active and independent[2,3]

CK-MB, creatine kinase-myocardial band; nmDMD, nonsense mutation Duchenne muscular dystrophy.

Patient photo is for illustrative purposes only.

The goal of treatment with Translarna is to slow the progression of nmDMD. Individual treatment results will vary.

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TREATMENT OUTCOME

Motor performance results during treatment with Translarna (40 mg/kg/day) over 16 months[8]

Motor performance test	At 21 months of age (prior to treatment intiation)	*Translarna initiated at 24 months of age*	At 32 months of age (8 months after treatment intiation)	At 40 months of age (16 months after treatment intiation)
North Star Ambulatory Assessment (NSAA)	10/34		19/34[a,b]	21/34[a,b]

[a]An average decline of 4.67 points can be expected for a boy with a mutation that occurs after exon 63 compared with those who have a mutation before exon 44, and a decline of 4.03 points can be expected compared with those who have a mutation between exons 44 and 62.[8]
[b]At 3 years and 4 months, this patient's NSAA score was higher than the average observed in a cohort of DMD patients of similar age (N=153; mean age = 4.68 years). In that cohort, average NSAA score was 16.33 for those treated with steroids and 13.64 for steroid-naive patients.[8]

After patient started treatment with Translarna at 2 years, his motor performance as measured by the NSAA improved[8]*

After 8 months of treatment:

- Muscle strength, upper limb movements, and motor skills in walking, jumping, and running improved significantly[8]
- Neurological examination still showed waddling gait, slight proximal muscle weakness, reduced deep tendon reflexes, partial Gowers' sign, and slight delay in neurodevelopment[8]

After 16 months of treatment:

- Patient was able to walk and rise on his own, with negative Gowers' sign, indicating a clear improvement in proximal lower limb muscle strength[8]
- No cardiac or respiratory changes were observed[8]

Translarna delayed loss of ambulation in real-world nmDMD patients, allowing patients to keep walking, for longer[2]

Treatments that delay the progression of nmDMD have the potential to **improve the HRQoL of individuals and their caregivers**[9-11]

Translarna is a generally well-tolerated oral therapy that has been received by **over 1640 patients**[1,12†]

Optimising therapy is achieved by dosing Translarna 3 times daily and regularly adjusting for changes in body weight[1,4]

The goal of treatment with Translarna is to slow the progression of nmDMD. Individual treatment results will vary.

Starting Translarna treatment at 2 years of age helped this patient preserve and improve muscle function.[8]*
Patients with nmDMD should be treated promptly to delay life-threatening disease progression.[1,3]

*Motor performance as measured by the NSAA is expected to increase in children <6 years of age during the natural course of the disease. Therefore, some improvement may be attributed to expected maturational effects in this age range.[8]
†The most frequent adverse reactions in the two placebo-controlled studies in patients aged ≥5 years were vomiting, diarrhoea, nausea, headache, upper abdominal pain, and flatulence. The majority of adverse reactions were mild or moderate in severity. One Translarna patient discontinued due to constipation, and one placebo patient discontinued due to loss of ambulation.[1] Safety data from 28 weeks of therapy showed a similar safety profile of Translarna in patients aged ≥2 to <5 years as compared with patients aged ≥5 years.[1] A higher frequency of malaise, pyrexia, ear infection, and rash were reported in patients aged ≥2 to <5 years, compared with patients 5 years of age and older. However, these conditions are reported more frequently in younger children in general.[1] Safety data from the STRIDE registry were consistent with the known safety profile of Translarna.[3]

HRQoL, health-related quality of life; nmDMD, nonsense mutation Duchenne muscular dystrophy.

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CASE 2: Importance of starting Translarna early

After Translarna initiation at 5 years of age, this boy's motor performance remained stable[13]

Patient case based on Ruggiero L et al. Ther Adv Neurol Disord. 2018;11(1):1–7.

INITIAL PRESENTATION

- At 4 years of age, **attention difficulties, Gowers' sign**, and **waddling gait** with hyperlordosis[13]
  - Also noted was pseudohypertrophy of the quadriceps and gastrocnemius muscles, with associated proximal weakness

DIAGNOSIS

- **Genetic testing** confirmed a diagnosis of **nmDMD**[13]
  - Mutation c.7471C>T, exon 51

TREATMENT HISTORY

- 5 years of age: **Translarna initiated** (40 mg/kg/day)[13]
  - Caregiver refused to start corticosteroid treatment
- 6 years of age: Follow-up mobility measures during 12-month treatment period[13]

Early and accurate diagnosis of nmDMD ensures that treatment can begin before patients permanently lose physical function[14]

Translarna is the first and only approved dystrophin restoration therapy in Europe addressing the underlying cause of nmDMD in ambulatory patients aged 2 years and older[1]

Translarna preserved physical function for longer than SoC alone in real-world nmDMD patients, enabling them to be more active and independent[2,3]

nmDMD, nonsense mutation Duchenne muscular dystrophy.

Patient photo is for illustrative purposes only.

The goal of treatment with Translarna is to slow the progression of nmDMD. Individual treatment results will vary.

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TREATMENT OUTCOME

Motor performance results during treatment with Translarna (40 mg/kg/day) over 1 year[13]

Motor performance test	Beginning of treatment	3 months	6 months	9 months	12 months
6MWT (metres)	320	330	355	409	400[a]
10-metre run/walk (seconds)	10	5.6	5.9	6.8	8.6[b]
Timed 4-stair ascent (seconds)	14	10	11	15	14
Timed 4-stair ascent (seconds)	9	9	10	9.7	10
Timed stand from supine (seconds)	4.5	5.6	4.2	5	7

[a]A decline of 50-117 metres per year in 6MWT can be expected, based on natural history studies in patients with DMD.[15]
[b]In a natural history study that included 6 boys <7 years of age, baseline 10-metre walk/run time was 4.8 seconds (SD: 0.86) and decreased by an average of 0.2 seconds over the 48-week study period.[16]

After patient started treatment with Translarna at 5 years, his motor performance remained the same or improved[13]

Over the 12-month treatment period:

- Patient's **6MWT increased** from 320 metres to 400 metres[13]
- Patient performance on the **10-metre walk/run test improved** (8.6 seconds vs 10 seconds at baseline)[13]

Improvement in HRQoL

According to his caregivers, this patient[13]:

- Had **less fatigue and improved QoL**
- Demonstrated **improvements in school performance**
- Spent more time on **social and entertainment-based activities**

Translarna delayed loss of ambulation in real-world nmDMD patients, allowing patients to keep walking, for longer[2]

Treatments that delay the progression of nmDMD have the potential to **improve the HRQoL of individuals and their caregivers**[9-11]

Translarna is a generally well-tolerated oral therapy that has been received by **over 1640 patients**[1,12*]

Optimising therapy is achieved by dosing Translarna 3 times daily and regularly adjusting for changes in body weight[1,4]

The goal of treatment with Translarna is to slow the progression of nmDMD. Individual treatment results will vary.

Starting Translarna treatment early helped this patient preserve physical function for longer.[14] Patients with DMD should be treated promptly to delay life-threatening disease progression.[1,3]

*The most frequent adverse reactions in the 2 placebo-controlled studies in patients aged ≥5 years were vomiting, diarrhoea, nausea, headache, upper abdominal pain, and flatulence. The majority of adverse reactions were mild or moderate in severity. One Translarna patient discontinued due to constipation, and one placebo patient discontinued due to loss of ambulation.[1] Safety data from 28 weeks of therapy showed a similar safety profile of Translarna in patients aged ≥2 to <5 years as compared with patients aged ≥5 years.[1] A higher frequency of malaise, pyrexia, ear infection, and rash were reported in patients aged ≥2 to <5 years, compared with patients 5 years of age and older. However, these conditions are reported more frequently in younger children in general.[1] Safety data from the STRIDE registry were consistent with the known safety profile of Translarna.[3]

6MWT, 6-minute walk test; DMD, Duchenne muscular dystrophy; HRQoL, health-related quality of life; nmDMD, nonsense mutation Duchenne muscular dystrophy; QoL, quality of life; SD, standard deviation.

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CASE 3: Translarna delayed decline in a severely impaired patient[13]

Translarna slowed the rate of motor function decline in an 8-year-old boy with severe clinical impairment[13]

Patient case based on Ruggiero L et al. Ther Adv Neurol Disord. 2018;11(1):1–7.

INITIAL PRESENTATION

- **Poor language ability** and mild cognitive impairment at 5 years of age[13]

DIAGNOSIS

- **Genetic testing** confirmed a diagnosis of **nmDMD**[13]
  - Mutation c.3242C>A, exon 24

TREATMENT HISTORY

- 5 years of age: corticosteroid (20 mg/day) initiated immediately after diagnosis[13]
- 7 years of age: **Translarna initiated** (40 mg/kg/day)[13]
  - Motor impairment was already very severe (6MWT <75 metres) prior to treatment
  - Presented with a **more severe clinical impairment** when compared with natural history studies*
- 8 years of age: Follow-up mobility measures during 12-month treatment period[13]

Early and accurate diagnosis of nmDMD is critical because once muscle function is lost, it cannot be restored[17-20]

Translarna is the first and only approved dystrophin restoration therapy in Europe addressing the underlying cause of nmDMD in ambulatory patients aged 2 years and older[1]

Translarna preserved physical function for longer than SoC alone in real-world nmDMD patients, enabling them to be more active and independent[2,3]

DMD, Duchenne muscular dystrophy; nmDMD, nonsense mutation Duchenne muscular dystrophy.

*The premature worsening of this patient's motor performance was due to inadequate surgical correction of a contracted Achilles tendon.[13]

Patient photo is for illustrative purposes only.

The goal of treatment with Translarna is to slow the progression of nmDMD. Individual treatment results will vary.

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TREATMENT OUTCOME

Motor performance results during treatment with Translarna (40 mg/kg/day) over 1 year[13]

Motor performance test	Beginning of treatment	3 months	6 months	9 months	12 months
6MWT (metres)	64	100	101	119	118[a]
10-metre run/walk (seconds)	30	19	22	16	17[b]

[a]A decline of 50-117 metres per year in 6MWT can be expected, based on natural history studies in patients with DMD.[15]
[b]In a natural history study that included 34 boys ≥7 years of age, baseline 10-metre walk/run time was 7.1 seconds (SD: 2.8) and increased by an average of 3.0 seconds over the 48-week study period.[16]

Patient's motor function was preserved above baseline, in contrast to the severe motor function decline expected for a DMD child of his age[13]

Over the 12-month treatment period:

- Patient's **6MWT was preserved at ≥100 metres at all time points over 12 months**[13]
- Patient performance on the **10-metre walk/run test was maintained above baseline** (17 seconds vs 30 seconds at baseline)[13]

Improvement in HRQoL

According to his caregivers, this patient[13]:

- Had **less fatigue and improved QoL**
- Demonstrated **improvements in school performance**
- Spent more time on **social and entertainment-based activities**

The goal of treatment with Translarna is to slow the progression of nmDMD. Individual treatment results will vary.

Translarna delayed loss of ambulation in real-world nmDMD patients, allowing patients to keep walking, for longer[2]

Treatments that delay the progression of nmDMD have the potential to **improve the HRQoL of individuals and their caregivers**[9-11]

Translarna is a generally well-tolerated oral therapy that has been received by **over 1640 patients**[1,12*]

Optimising therapy is achieved by dosing Translarna 3 times daily and regularly adjusting for changes in body weight[1,4]

In this patient with severe impairment, Translarna helped delay motor function decline.[13] The totality of evidence consistently demonstrates the efficacy of Translarna in nmDMD in clinical trials and the real world.[2-6]

*The most frequent adverse reactions in the 2 placebo-controlled studies in patients aged ≥5 years were vomiting, diarrhoea, nausea, headache, upper abdominal pain, and flatulence. The majority of adverse reactions were mild or moderate in severity. One Translarna patient discontinued due to constipation, and one placebo patient discontinued due to loss of ambulation.[1] Safety data from 28 weeks of therapy showed a similar safety profile of Translarna in patients aged ≥2 to <5 years as compared with patients aged ≥5 years.[1] A higher frequency of malaise, pyrexia, ear infection, and rash were reported in patients aged ≥2 to <5 years, compared with patients 5 years of age and older. However, these conditions are reported more frequently in younger children in general.[1] Safety data from the STRIDE registry were consistent with the known safety profile of Translarna.[3]

6MWT, 6-minute walk test; DMD, Duchenne muscular dystrophy; HRQoL, health-related quality of life; nmDMD, nonsense mutation Duchenne muscular dystrophy; QoL, quality of life; SD, standard deviation.

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CASE 4: Translarna helped preserve motor function for longer[13]

Translarna treatment **maintained motor performance for longer** for this 11-year-old boy diagnosed with nmDMD[13]

Patient case based on Ruggiero L et al. Ther Adv Neurol Disord. 2018;11(1):1–7.

INITIAL PRESENTATION

- **Elevated liver enzymes** were detected in the absence of liver function impairment at 5 years of age, prompting the patient's first neurological examination[13]
  - Past medical history had been uneventful, with normal milestones

DIAGNOSIS

- **A creatine kinase (CK) test** showed that levels were **markedly increased** (>10,000 U/L)[13]
- **Genetic testing** confirmed a diagnosis of **nmDMD**[13]
  - Mutation c.2077T>C, exon 17

TREATMENT HISTORY

- 5 years of age: corticosteroid (15 mg/day) initiated immediately after diagnosis[13]
  - Discontinued due to poor tolerability (agitation and sleep alterations) at 7 years of age
- 10 years of age: **Translarna initiated** (40 mg/kg/day)[13]
  - Baseline 6MWT was 360 metres*
- 11 years of age: Follow-up mobility measures during 12-month treatment period[13]

Timely and accurate diagnosis of nmDMD enables patients and families to receive care and support needed to improve QoL[18,19,21]

Translarna is the first and only approved dystrophin restoration therapy in Europe addressing the underlying cause of nmDMD in ambulatory patients aged 2 years and older[1]

Translarna preserved physical function for longer in real-world nmDMD patients, enabling them to be more active and independent[2,3]

6MWT, 6-minute walk test; nmDMD, nonsense mutation Duchenne muscular dystrophy; QoL, quality of life.

*This patient's good performance on the 6MWT—despite his age and absence of steroid treatment—may be explained by a faint reaction of dystrophin or revertant fibers in his muscle biopsy.[13]

Patient photo is for illustrative purposes only.

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TREATMENT OUTCOME

Motor performance results during treatment with Translarna (40 mg/kg/day) over 1 year[13]

Motor performance test	Beginning of treatment	3 months	6 months	9 months	12 months
6MWT (metres)	360	303	375	400	370[a]
10-metre run/walk (seconds)	10	6.5	7.5	6.7	7.5[b]
Timed 4-stair ascent (seconds)	7.0	7.2	7.5	8.3	7.6
Timed 4-stair ascent (seconds)	4.5	6.1	5.2	5.5	5.5
Timed stand from supine (seconds)	35	26	25	16	44

[a]A decline of 50-117 metres per year in 6MWT can be expected, based on natural history studies in patients with DMD.[15]
[b]In a natural history study that included 34 boys ≥7 years of age, baseline 10-metre walk/run time was 7.1 seconds (SD: 2.8) and increased by an average of 3.0 seconds over the 48-week study period.[16]

After 12 months of treatment with Translarna, patient's disease remained stable, as shown by motor performance[13]

- Patient's **6MWT increased** from 360 metres to 370 metres[13]
- Patient performance on the **10-metre walk/run test improved** (7.5 seconds vs 10 seconds at baseline)[13]

Improvement in HRQoL
According to his caregivers, this patient[13]:

- Had **less fatigue and improved QoL**
- Demonstrated **improvements in school performance**
- Spent more time on **social and entertainment-based activities**

Translarna delayed loss of ambulation in real-world nmDMD patients, allowing patients to keep walking, for longer[2]

Treatments that delay the progression of nmDMD have the potential to **improve the HRQoL of individuals and their caregivers**[9-11]

Translarna is a generally well-tolerated oral therapy that has been received by **over 1640 patients**[1,12*]

Optimising therapy is achieved by dosing Translarna 3 times daily and regularly adjusting for changes in body weight[1,4]

The goal of treatment with Translarna is to slow the progression of nmDMD. Individual treatment results will vary.

With Translarna treatment, this patient's disease remained stable as measured by motor performance.[13] The totality of evidence consistently demonstrates the efficacy of Translarna in nmDMD clinical trials and the real world.[2-6]

*The most frequent adverse reactions in the 2 placebo-controlled studies in patients aged ≥5 years were vomiting, diarrhoea, nausea, headache, upper abdominal pain, and flatulence. The majority of adverse reactions were mild or moderate in severity. One Translarna patient discontinued due to constipation, and one placebo patient discontinued due to loss of ambulation.[1] Safety data from 28 weeks of therapy showed a similar safety profile of Translarna in patients aged ≥2 to <5 years as compared with patients aged ≥5 years.[1] A higher frequency of malaise, pyrexia, ear infection, and rash were reported in patients aged ≥2 to <5 years, compared with patients 5 years of age and older. However, these conditions are reported more frequently in younger children in general.[1] Safety data from the STRIDE registry were consistent with the known safety profile of Translarna.[3]

6MWT, 6-minute walk test; DMD, Duchenne muscular dystrophy; HRQoL, health-related quality of life; nmDMD, nonsense mutation Duchenne muscular dystrophy; QoL, quality of life; SD, standard deviation.

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CASE 5: Importance of continual Translarna treatment

Translarna **delayed loss of ambulation** for this 16-year-old boy diagnosed with nmDMD at 18 months of age[22]

Patient case based on Mercuri E et al. Eur Neurol Rev. 2018;13(1):31–37.

INITIAL PRESENTATION

- **Motor delay** at 18 months of age[22]

DIAGNOSIS

- **Increased creatine kinase levels** (9249 IU/L)[22]
- Subsequent **muscle biopsy** confirmed **absence of dystrophin**[22]
- **Genetic testing** confirmed a diagnosis of **nmDMD**[22]
  - Mutation c.8069T>G, exon 55

TREATMENT HISTORY

- 6 years of age: daily prednisolone and vitamin D[22]
- 9 years of age: **Translarna initiated** when patient was a participant in a phase 2b clinical trial[22]*
- 13 years, 8 months: **Translarna was resumed**[22]
  - Patient was ambulant with a waddling gait
  - Concomitant medications included testosterone, vitamin D, and low-dose prednisolone
  - Echocardiography showed left ventricular fractional shortening (23% to 27%) and mild left ventricular hypokinesia/dyskinesia; perindopril was prescribed

Early diagnosis and proper management of nmDMD is expected to improve QoL for patients and caregivers[18,20,21,23]

Translarna is the first and only approved dystrophin restoration therapy in Europe addressing the underlying cause of nmDMD in ambulatory patients aged 2 years and older[1]

Translarna preserved physical function for longer in real-world nmDMD patients, enabling them to be more active and independent[2,3]

DMD, Duchenne muscular dystrophy; nmDMD, nonsense mutation Duchenne muscular dystrophy; QoL, quality of life.

*During the trial, the patient suffered a bone fracture and discontinued Translarna; however, he made a full recovery.[22]

Patient photo is for illustrative purposes only.

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TREATMENT OUTCOME

Motor performance results during treatment with Translarna (40 mg/kg/day) over 3 years[22]

Motor performance test	Treatment initiation (13 years and 8 months old)	Time of report (16 years and 8 months old)
Six-minute walk test (6MWT) (metres)	315	166 (↓ *of 149 metres after treatment with Translarna*[a])
North Star Ambulatory Assessment score (NSAA)	15	4 (↓ *of 11 units [~3.7/year]after treatment with Translarna*[b])

[a]A decline of 50-117 metres per year in 6MWT can be expected, based on natural history studies in patients with DMD. Based on these data, this patient could have expected a decline of 150 to 351 metres over 3 years versus 149 metres seen in this case.[15]
[b]On average, the NSAA score decreases by 3 units per year. Based on these data, this patient could have expected a decrease of 9 units over 3 years versus 11 units seen in this case.[24]

After 3 years of Translarna treatment, patient was able to remain ambulant[22]

- Patient had cardiac issues prior to starting treatment with Translarna[22]
- Repeat echocardiography showed normal cardiac function after use of an ACE inhibitor during concomitant treatment with Translarna, which maintained his ambulation for longer[22]
- Patient remained ambulant at 16 years and 8 months, in contrast to natural history data for boys with DMD that indicates the average age for loss of ambulation is 12.3 years[22]

Translarna delayed loss of ambulation in real-world nmDMD patients, allowing patients to keep walking, for longer[2]

Treatments that delay the progression of nmDMD have the potential to **improve the HRQoL of individuals and their caregivers**[9-11]

Translarna is a generally well-tolerated oral therapy that has been received by **over 1640 patients**[1,12*]

Optimising therapy is achieved by dosing Translarna 3 times daily and regularly adjusting for changes in body weight[1,4]

The goal of treatment with Translarna is to slow the progression of nmDMD. Individual treatment results will vary.

Continual dosing with Translarna helped this patient remain ambulant 5 years longer than expected.[22]
Correct dosing of Translarna ensures optimal therapeutic benefit.[1,4,25]

*The most frequent adverse reactions in the 2 placebo-controlled studies in patients aged ≥5 years were vomiting, diarrhoea, nausea, headache, upper abdominal pain, and flatulence. The majority of adverse reactions were mild or moderate in severity. One Translarna patient discontinued due to constipation, and one placebo patient discontinued due to loss of ambulation.[1] Safety data from 28 weeks of therapy showed a similar safety profile of Translarna in patients aged ≥2 to <5 years as compared with patients aged ≥5 years.[1] A higher frequency of malaise, pyrexia, ear infection, and rash were reported in patients aged ≥2 to <5 years, compared with patients 5 years of age and older. However, these conditions are reported more frequently in younger children in general.[1] Safety data from the STRIDE registry were consistent with the known safety profile of Translarna.[3]

ACE, angiotensin-converting enzyme; HRQoL, health-related quality of life; nmDMD, nonsense mutation Duchenne muscular dystrophy.

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Translarna slows disease progression and preserves ambulation for longer compared to SoC alone in real-world patients with nmDMD

In a real-world setting, patients with nmDMD in the STRIDE Registry were compared with propensity score-matched patients with DMD in CINRG DNHS.[2,3]* The data showed that:

Translarna delayed loss of ambulation in real-world nmDMD patients, allowing patients to keep walking for longer[2†]

Translarna could delay pulmonary function decline in nmDMD patients[3§]

Translarna + SoC preserved physical function for longer vs treatment with SoC alone, allowing boys with nmDMD to be more active and independent[3‡]

Translarna is a generally well-tolerated oral therapy that has been received by **over 1640 patients**[1,13‖]

The goal of treatment with Translarna is to slow the progression of nmDMD. Individual treatment results will vary.

Translarna is the first and only approved dystrophin restoration therapy addressing the underlying cause of nmDMD in Europe in ambulatory patients aged 2 years and older.[1]

*As of 31 January, 2022, 261 nmDMD patients from the STRIDE Registry were individually matched with 261 DMD patients from CINRG DNHS using established measures of disease progression (age at first clinical symptoms, age at first corticosteroid use, duration of deflazacort use, duration of other corticosteroid use). An acknowledged limitation of this analysis is that populations were not matched according to mutation type or location. SoC refers to corticosteroids (deflazacort, prednisolone, and prednisone) and palliative therapies.[2] CINRG DNHS is the largest natural history study to date in DMD and represents a real-world control group for comparison with STRIDE. Patients were followed closely for several years: median treatment follow-up was 1796 days.[3,7] †Translarna + SoC provided 4.0 years of additional ambulation vs SoC alone. Median age at loss of ambulation: 17.0 years (STRIDE) vs 13.0 years (CINRG DNHS), HR 0.375 (95% CI: 0.277, 0.508); p<0.0001.[2] ‡As measured by time to climb four stairs and time to stand from supine. Median age at worsening of time to climb four stairs to ≥10 seconds: milestone not reached (STRIDE) vs 13.2 years (CINRG DNHS). HR (95% CI): 0.385 (95% CI: 0.172, 0.859); p=0.0195. Median age at worsening of time to stand from supine to ≥10 seconds: STRIDE 14.0 years, CINRG DNHS 9.9 years. HR 0.290 (95% CI: 0.140, 0.642); p=0.0008.[3] §Study authors note that there is a trend towards delayed worsening of pulmonary function but that due to short duration of follow-up and low number of events, it is premature to draw firm conclusions from these results.[3] ‖The most frequent adverse reactions in the two placebo-controlled studies in patients aged ≥5 years were vomiting, diarrhoea, nausea, headache, upper abdominal pain, and flatulence. The majority of adverse reactions were mild or moderate in severity. One Translarna patient discontinued due to constipation, and one placebo patient discontinued due to loss of ambulation.[1] Safety data from 28 weeks of therapy showed a similar safety profile of Translarna in patients aged ≥2 to <5 years as compared with patients aged ≥5 years.[1] A higher frequency of malaise, pyrexia, ear infection, and rash were reported in patients aged ≥2 to <5 years, compared with patients 5 years of age and older. However, these conditions are reported more frequently in younger children in general.[1] Safety data from the STRIDE registry were consistent with the known safety profile of Translarna.[3]

CI, confidence interval; CINRG DNHS, Cooperative International Neuromuscular Research Group Duchenne Natural History Study; DMD, Duchenne muscular dystrophy; HR, hazard ratio; nmDMD, nonsense mutation Duchenne muscular dystrophy; SoC, standard of care; STRIDE, Strategic Targeting of Registries and International Database of Excellence.

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Registration conditions differ internationally, always consult local prescribing information and/or Summary of Product Characteristics before prescribing any product. For the EU Translarna Summary of Product Characteristics, **please click here.**

▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system. Adverse events should also be reported to PTC Therapeutics at pharmacovigilance@ptcbio.com

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Abbreviated Prescribing Information Indication: Translarna™ (active ingredient: ataluren) is indicated for the treatment of Duchenne muscular dystrophy resulting from a nonsense mutation in the dystrophin gene (nmDMD), in ambulatory patients aged 2 years and older. The presence of a nonsense mutation in the dystrophin gene should be determined by genetic testing. **Posology and administration:** Translarna is available as granules for oral suspension in sachets of 125 mg, 250 mg or 1000 mg. The recommended dose is 10 mg/kg body weight in the morning, 10 mg/kg body weight at midday, and 20 mg/kg body weight in the evening (for a total daily dose of 40 mg/kg body weight). Patients should not take a double or extra dose if a dose is missed. It is important to administer the correct dose. Increasing the dose above the recommended dose may be associated with reduced effectiveness. Treatment of patients with severe renal impairment (eGFR <30 ml/min) or end-stage renal disease is not recommended. The safety and efficacy of Translarna in children <12kg and aged 6 months to 2 years have not yet been established. Treatment with Translarna should only be initiated by specialist physicians with experience in the management of DMD. **Ingredients:** Active ingredient: ataluren. **Excipients:** polydextrose (E1200), macrogol, poloxamer, mannitol (E421), crospovidone, hydroxyethyl cellulose, artificial vanilla flavour (maltodextrin, artificial flavours and propylene glycol), silica, colloidal anhydrous (E551), magnesium stearate. Contraindications: Patients with hypersensitivity to the active substance or to any of the excipients; concomitant use of intravenous aminoglycosides. **Special warnings and precautions for use:** Patients who do not have a nonsense mutation should not receive Translarna. Patients with severe renal impairment or end-stage renal disease should be treated with ataluren only if the anticipated clinical benefit outweighs the potential risk, and should be closely monitored for possible metabolite toxicity and decrease in efficacy. A lower ataluren dose should be considered. Treatment should not be initiated in previously untreated patients with eGFR <30 ml/min. It is recommended that total cholesterol, LDL, HDL, triglycerides be measured annually, and serum creatinine, BUN, cystatin C be measured every 6 to 12 months. Resting systolic and diastolic blood pressure should be monitored every 6 months in patients receiving Translarna concomitantly with corticosteroids. All clinical measures and/ or laboratory testing may be conducted more frequently as needed based on clinical status. See precaution for use with other medicines in next “interactions” section. **Interactions:** Translarna should not be co-administered with intravenous aminoglycosides, and concomitant use of other nephrotoxic agents is not recommended. Caution should be exercised when Translarna is co-administered with medicinal products that are inducers of UGT1A9, or substrates of OAT1, OAT3 or OATP1B3 and when co-administered with adefovir. Based on in vitro studies Translarna is not expected to be an inducer of P450 isoenzymes. **Fertility, pregnancy and lactation:** It is recommended to avoid the use of Translarna in pregnancy. Breast-feeding should be discontinued during treatment with Translarna. Non-clinical data revealed no hazard for humans based on standard male and female fertility study in rats. **Effects on ability to drive and use machines:** Patients who experience dizziness should use caution when driving, cycling or using machines. Adverse reactions: Adverse events reported in clinical trials of predominantly paediatric nmDMD patients treated at the recommended dose of 10-, 10-, 20mg/kg/day according to frequency: Very common (≥1/10): vomiting. Common (≥1/100 to <1/10): decreased appetite, hypertriglyceridemia, headache, hypertension, cough, epistaxis, nausea, upper abdominal pain, flatulence, abdominal discomfort, constipation, rash erythematous, pain in extremity, musculoskeletal chest pain, haematuria, enuresis, pyrexia, weight decreased. Events with unknown frequency due to low numbers: increased blood urea nitrogen, cholesterol, creatinine, cystatin C, triglycerides. **Marketing Authorisation number and holder:** EU/1/13/902/001-002-003. PTC Therapeutics International Limited, 5th Floor, 3 Grand Canal Plaza, Grand Canal Street Upper, Dublin 4, Ireland. Please consult the SmPC before prescribing. **Date of Preparation:** June 2022.

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