Applied Therapeutics

SORD 12 Month Interim Data Analysis

March 2024

APPLIED THERAPEUTICS

Forward Looking Statements

Various statements in this presentation concerning the Company's future expectations, plans and prospects constitute forward-looking statements. The use of words such as "may," "might," "will," "should," "expect," "plan," "anticipate," "believe," "estimate," "project," "intend," "future," "potential," or "continue," the negative of these and other similar expressions are intended to identify such forward looking statements. Such statements, based as they are on the current analysis and expectations of management, inherently involve numerous risks and uncertainties, known and unknown, many of which are beyond the Company's control. Such risks include, but are not limited to: the impact of general economic conditions, general conditions in the biopharmaceutical industries, changes in the global and regional regulatory environments in the jurisdictions in which the Company does or plans to do business, market volatility, fluctuations in costs and changes to the competitive environment, the Company's ability to fund its working capital requirements and expectations regarding the sufficiency of our capital resources and the Company's ability to achieve the anticipated benefits from the agreements entered into in connection with our partnership with Advanz Pharma. Consequently, actual future results may differ materially from the anticipated results expressed in the forward-looking statements. In the case of forward-looking statements regarding investigational product candidates and continuing further development efforts, specific risks which could cause actual results to differ materially from the Company's current analysis and expectations include: failure to demonstrate the safety, tolerability and efficacy of our product candidates; final and quality controlled verification of data and the related analyses; the expense and uncertainty of obtaining regulatory approval, including from the U.S. Food and Drug Administration and European Medicines Agency; the possibility of having to conduct additional clinical trials and our reliance on third parties such as our licensors and collaboration partners regarding our suite of technologies and product candidates; the Company's ability to take advantage of expedited regulatory pathways for any of our product candidates; the Company's intellectual property position and the duration of its patent rights; developments or disputes concerning the Company's intellectual property or other proprietary rights. Further, even if regulatory approval is obtained, biopharmaceutical products are generally subject to stringent on-going governmental regulation, challenges in gaining market acceptance and competition.

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INSPIRE Trial 12 Month Interim Topline Data

Co-primary endpoints at 12 month analysis:

- **Primary clinical efficacy endpoint**: Statistically significant correlation between sorbitol levels and change in clinical outcomes at 12 months of treatment on combined measures of the CMT Functional Outcome Measures (CMT-FOM) lower limb domain (10 meter walk-run test, 4 stair climb, and sit to stand test), 6-minute walk test and dorsiflexion ($p=0.05$)
- **Primary pharmacodynamic/ biomarker endpoint**: Sustained reduction in sorbitol level in patients treated with govorestat at 12 months, which was statistically significant compared to placebo ($p<0.001$).

Secondary Endpoints

- Highly statistically significant effect ($p=0.01$) impact of govorestat on the CMT Health Index (CMT-HI), an important patient-reported outcome measure of disease severity and well-being; aspects of the CMT-HI that demonstrated a treatment effect included lower limb function, mobility, fatigue, pain, sensory function, and upper limb function.
- Trends (not statistically significant) on CMT-FOM measures linked to walking ability, such as 10MWR, dorsiflexion and 6 minute walk test
    - No substantial effect on stair climb or sit-to-stand test

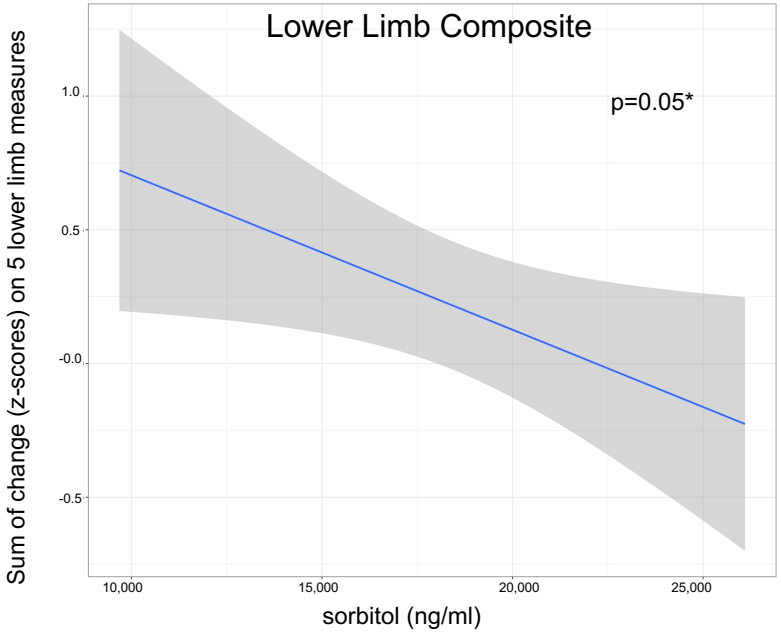
Safety

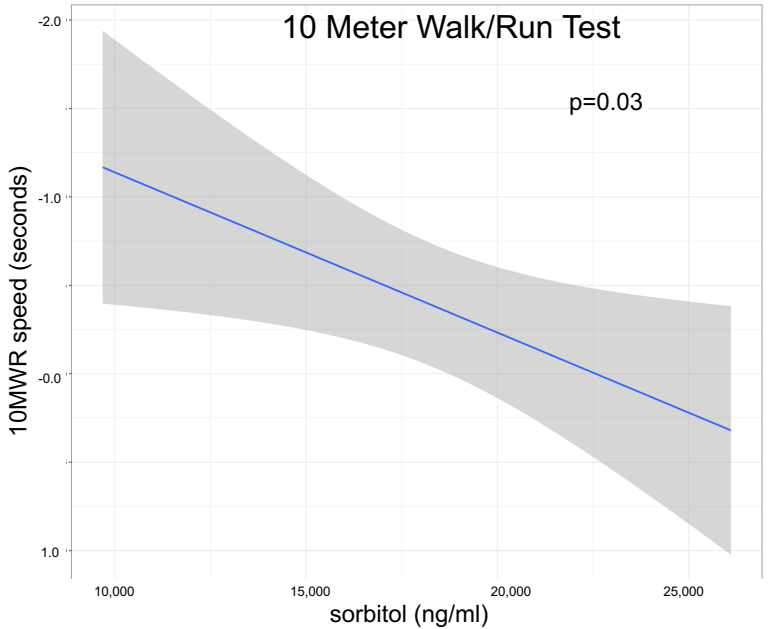
- Govorestat was safe and well tolerated, with similar incidence of adverse events between active and placebo-treated groups

Study will continue in blinded format to 24 months

Correlation of Sorbitol with CMT-FOM Lower Limb Measures

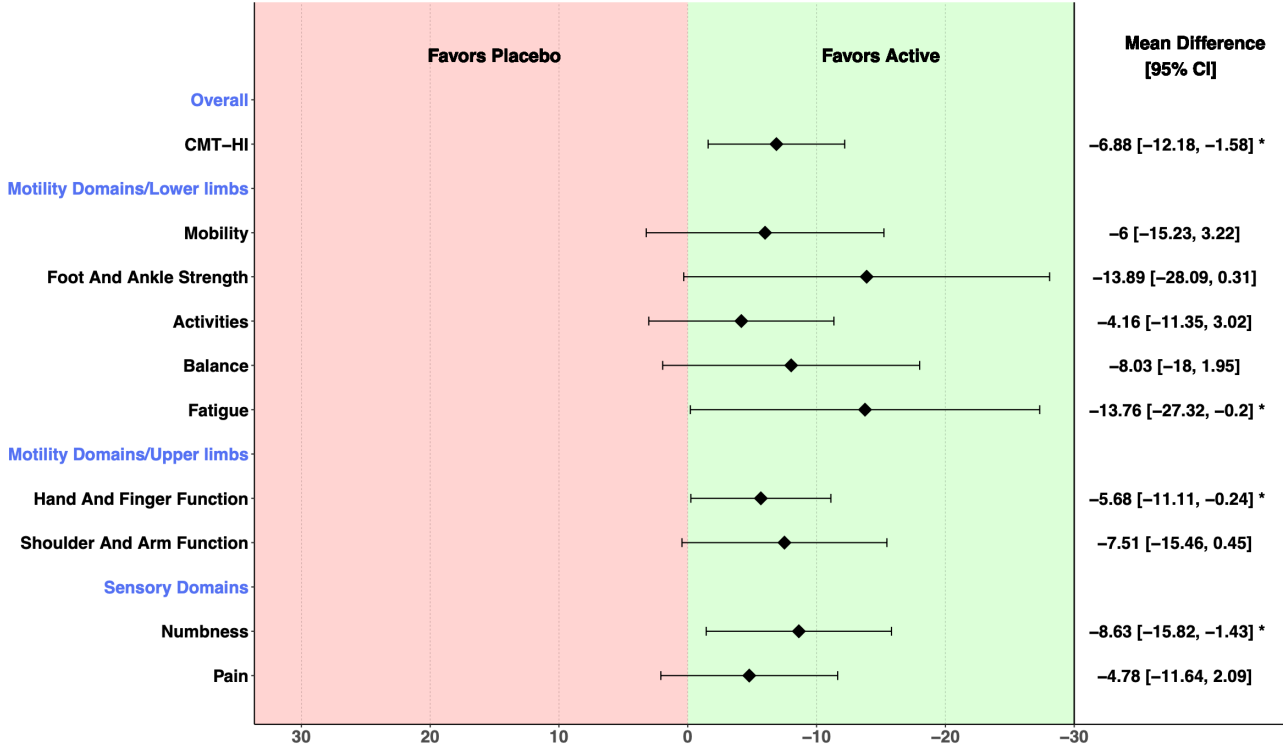
Lower sorbitol level at 12 months correlated with greater improvement in clinical outcomes (sum of change from baseline to 12 months across 10MWR, 4 stair climb, sit-to-stand test, 6-minute walk, dorsiflexion)





- Correlation analysis performed on govorestat treated patients
- *improved to p=0.03 when 3 patients with major protocol deviations were removed from analysis
- Directionality of 10MWR and 4-stair climb was flipped so that improvement aligned with other tests
- Statistical threshold defined as p<0.10 in statistical analysis plan

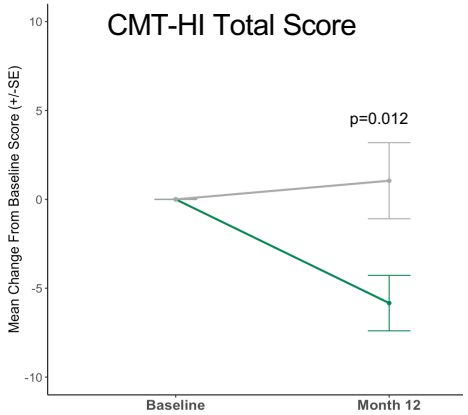
Govorestat Treated Patients Demonstrated a Statistically Significant Improvement in CMT-Health Index (CMT-HI) Scores at 12 Months (p=0.01 vs. placebo)

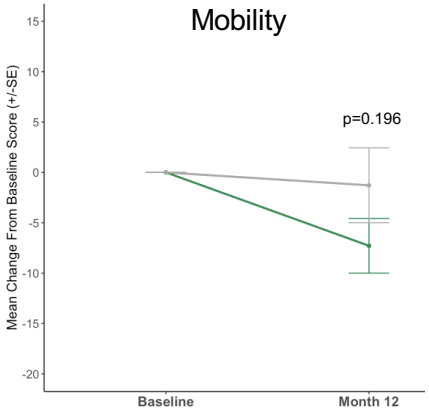


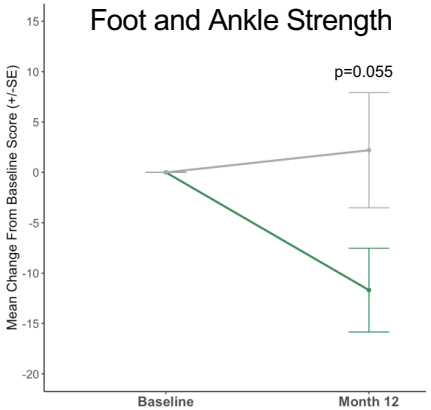
Lower score (negative change from baseline) represents improvement in disease symptoms; measures with “8” were statistically significant vs. placebo with p<0.05

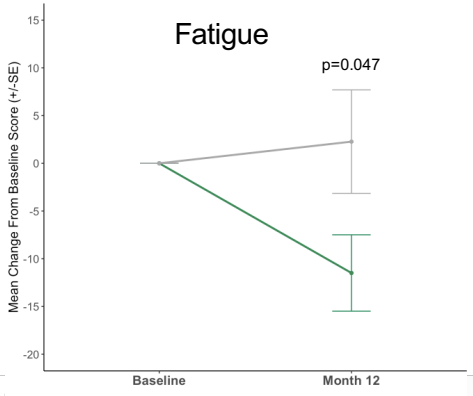
CMT-HI Change from Baseline at 12 Months (Lower Score is Improvement)

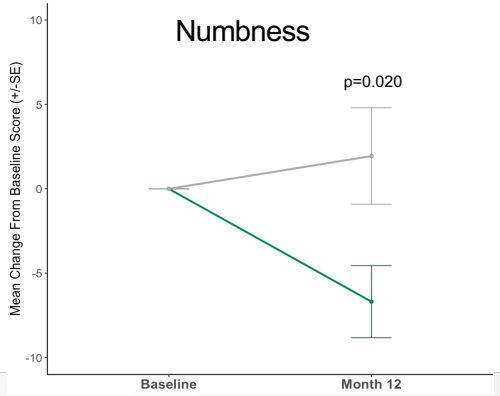
Govorestat treated group improved over 12 months, while placebo group generally worsened

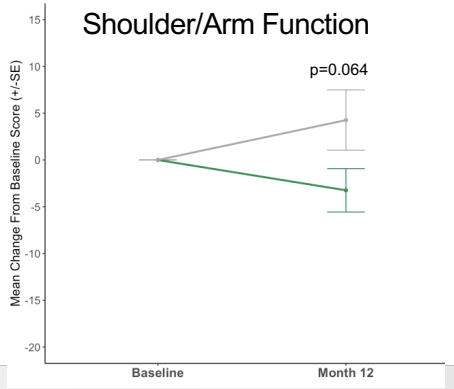








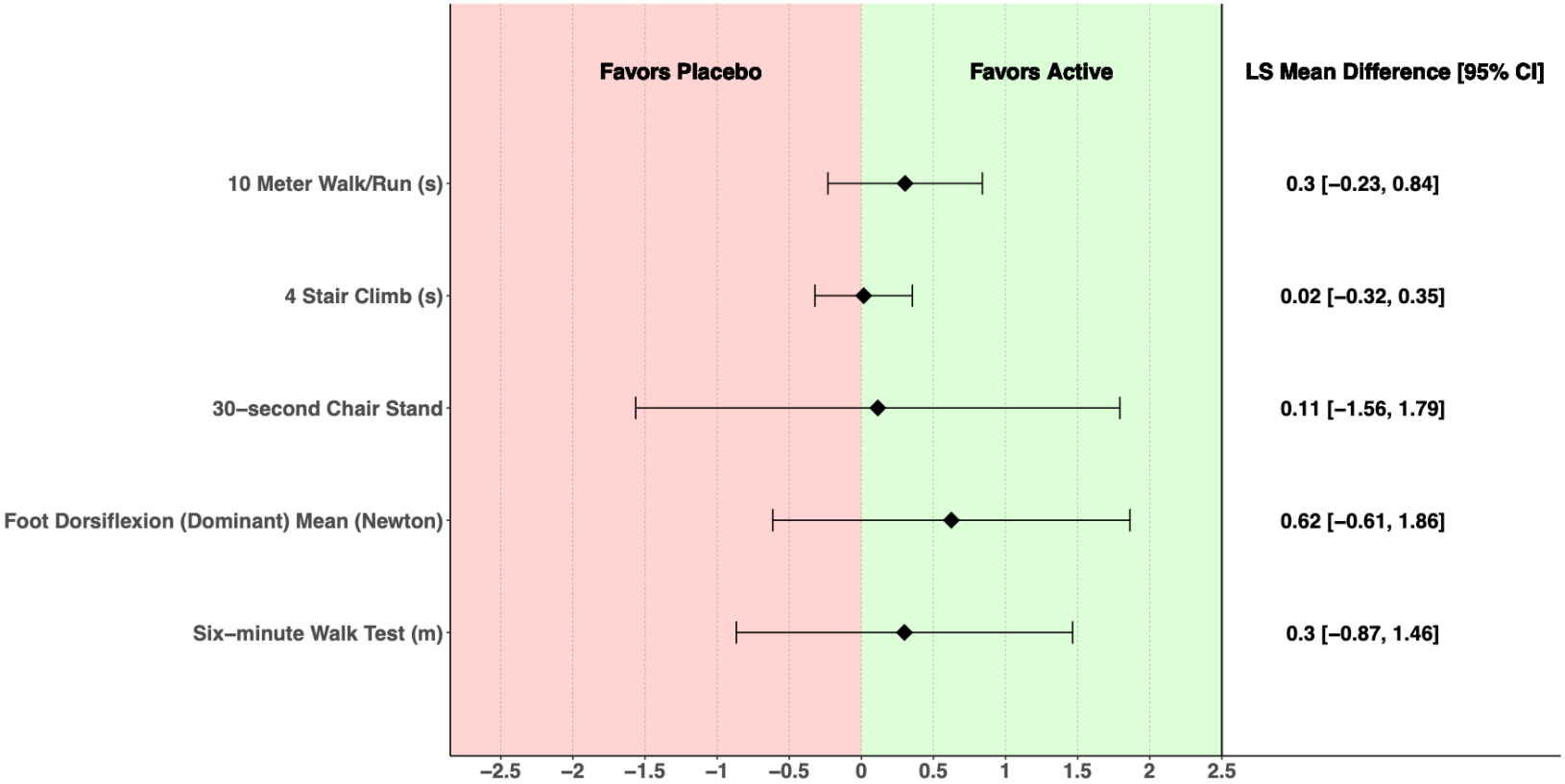




APPLIED THERAPEUTICS

AT-007 Placebo

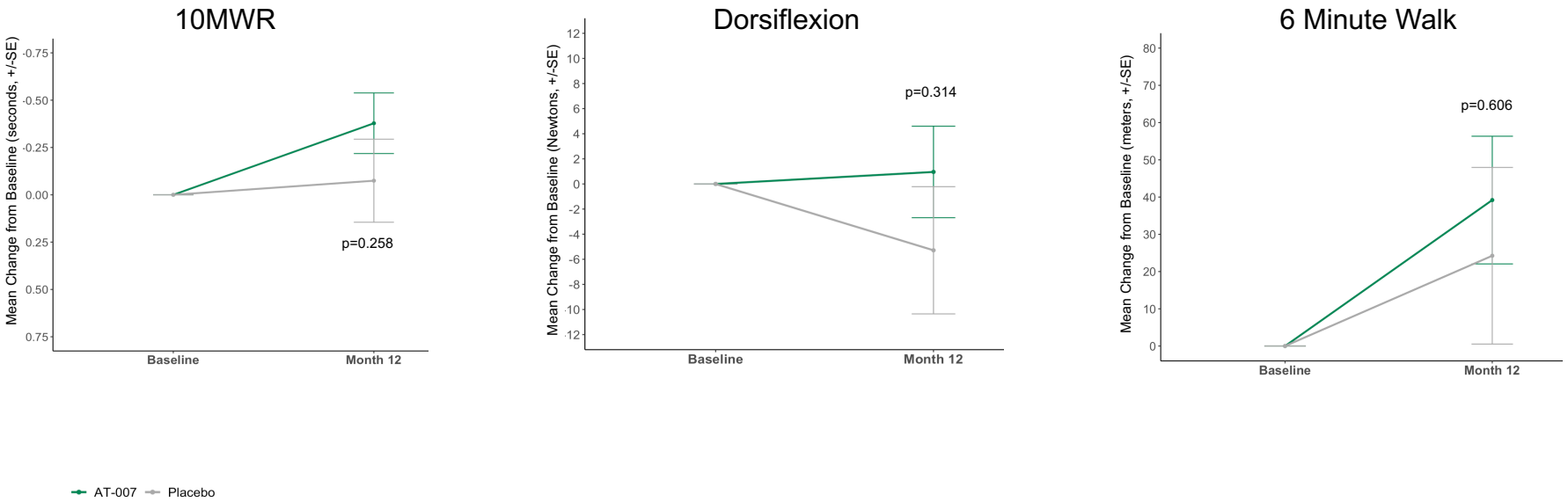
Govorestat Treated Patients Demonstrated Trend Towards Improvement in 10MWR, Dorsiflexion and 6 Minute Walk at 12 Months



For foot Dorsiflexion, the estimate and the CI were divided by 10 in order to present within the x−axis range (actual values are 10X the values on the slide); For 6-minute walk, the estimate and the CI were divided by 50 in order to present within the x−axis range (actual values are 50X the values on the slide). For 10 Meter Walk/Run and 4 Stair Climb, the 'change from baseline' value has been reversed (multiplied by -1) in order to maintain consistency of direction of interpretation in the forest plot

CMT-FOM Change from Baseline at 12 Months

Govorestat treated group improved compared to placebo on 10MWR, dorsiflexion and 6 minute walk; no effect on 4-stair climb or sit-to-stand test (not shown)



Baseline Demographics

		Placebo N=18 n (%)	Govorestat N=38 n (%)	Combined N=56 n (%)
Age Mean (SD)		36.0 (9.23)	33.6 (11.70)	34.4 (10.94)
BMI Mean (SD)		23.9 (3.57)	24.3 (4.15)	24.2 (3.94)
Race	White	16 (88.9%)	36 (94.7%)	52 (92.9%)
	Asian	1 (5.6%)	1 (2.6%)	2 (3.6%)
	Black	1 (5.6%)	0 (0.0%)	1 (1.8%)
	Other	0 (0.0%)	1 (2.6%)	1 (1.8%)
Sex	Male	12 (66.7%)	25 (65.8%)	37 (66.1%)
	Female	6 (33.3%)	13 (34.2%)	19 (33.9%)
Stage of Disease Progression (defined by 10MWR speed at baseline)	Mild (≤5s)	12 (66.7%)	23 (60.5%)	35 (62.5%)
	Moderate (5.1-7.5s)	3 (16.7%)	9 (23.7%)	12 (21.4%)
	Severe (7.6-15s)	3 (16.7%)	6 (15.8%)	9 (16.1%)
Sorbitol*		27,971ng/ml (SD=5,950)	30,934ng/ml (SD=4,360)	29,965ng/ml (SD=5,074)

*For sorbitol values at baseline N=52, as samples for 4 patients were missing (not processed correctly)

Patient Disposition

	Placebo N=18 n (%)	Govorestat N=38 n (%)	Combined N=56 n (%)
Randomized	18 (100.0%)	38 (100.0%)	56 (100.0%)
Ongoing	17 (94.4%)	34 (89.5%)	51 (91.1%)
Discontinued	1 (5.6%)	4 (10.5%)	5 (8.9%)
Reason for Discontinuation: Adverse Event	0 (0.0%)	3 (7.9%)	3 (5.4%)
Reason for Discontinuation: Withdrawal By Subject	1 (5.6%)	1 (2.6%)	2 (3.6%)

Safety

Safe and well-tolerated; adverse events were well-balanced between govorestat and placebo treated groups

	Placebo (N=18) n (%)	Govorestat (N=38) n (%)	Overall (N=56) n (%)
Treatment Emergent Adverse Events (number of patients reporting any adverse event during the study)[1]	15 (83.3%)	34 (89.5%)	49 (87.5%)
Mild	12 (66.7%)	33 (86.8%)	45 (80.4%)
Moderate	5 (27.8%)	8 (21.1%)	13 (23.2%)
Severe	0 (0.0%)	1 (2.6%)[2]	1 (1.8%)[2]
Serious Adverse Events	0 (0.0%)	1 (2.6%)[3]	1 (1.8%)[3]
Deaths	0 (0.0%)	0 (0.0%)	0 (0.0%)

1.Some patients reported more than one adverse event, so the sum of mild, moderate and severe is larger than the number of patients reporting an adverse event; 2. The severe adverse event was a recurrence of a pre-existing condition; 3. The serious adverse event was a motorcycle accident.