Sponsor

Novartis

Generic Drug Name

AFQ056

Therapeutic Area of Trial

L-dopa induced dyskinesia in Parkinson's disease (PD-LID)

Approved Indication

None

Protocol Number

CAFQ056A2222

Title

12-week, double-blind, placebo-controlled, fixed-dose, multi-centered study to evaluate the efficacy and safety of AFQ056 in reducing moderate to severe L-dopa induced dyskinesias in patients with Parkinson's disease

Phase of Development

Phase II

Study Start/End Dates

07-Nov-2011 to 14-Sep-2012

Study Design/Methodology

This study used a randomized, double-blind, placebo-controlled, fixed-dose, parallel-group design to evaluate the safety and efficacy of AFQ056 100 milligrams (mg) b.i.d. (twice daily) compared to placebo in patients with moderate to severe PD-LID.

The screening epoch was used to assess eligibility and to discontinue prohibited medications. The screening visit occurred 7-28 days before the Baseline (BL) 1 visit. At the BL1 visit, eligible patients entered a 2-week, single-blind, placebo run-in epoch, during which the patients and their caregivers were not aware that the patient was receiving placebo, but the clinician was unblinded to the medication status. During this epoch, patients underwent two baseline visits (baseline 1, baseline 2), which were used to characterize the patient's parkinsonian movement disorder, motor fluctuations, and dyskinesias. During this epoch, investigators ensured patients were on stable concomitant medications and assessed patient compliance with study procedures, including ability to provide accurate diary ratings of motor fluctuations and dyskinesias as per study inclusion criterion.

Patients who successfully completed the placebo run-in epoch then entered the 12-week double-blind treatment epoch where they were randomly assigned to AFQ056 100 mg b.i.d. or placebo treatment groups in a ratio of 4:3. Patients were titrated at two-week intervals until they reach the target dose of 100 mg b.i.d. After patients reached the target dose of 100 mg b.i.d., patients remained on this dose until they reached the end of the 12-week double-blind

treatment epoch. However, if the target dose was not maintained due to tolerability issues, patients were given the option to down-titrate to a lower dose of 75 mg b.i.d. Patients who completed the 12-week double-blind treatment epoch without major protocol deviations had the option to enroll into an open-label, long-term safety study.

Centers

28 sites in 7 countries: Germany (10), Spain (4), United States (2), Canada (1), France (4), Hungary (3), Italy (4)

Publication

None

Test Product(s), Dose(s), and Mode(s) of Administration

- AFQ056
- Dosage form: Hard gelatin capsules of 10 mg, 25 mg, 50 mg, 75 mg, 100 mg.
- Presentation: Capsules in bottles

Reference Product(s), Dose(s), and Mode(s) of Administration

- Placebo
- Dosage form: Hard gelatin capsules
- Presentation: Capsules in bottles

Statistical Methods

The primary and secondary efficacy analyses were performed on the Full Analysis Set (FAS), which consisted of all randomized patients who received at least one dose of double-blind study drug and had both a baseline and at least one post-baseline efficacy assessment during the double-blind treatment epoch.

The primary efficacy variable was the change from baseline 2 to Week 12 on the Modified Abnormal Involuntary Movement Scale (mAIMS) total score. The primary efficacy variable was analyzed using a mixed-effect repeated measure model (MMRM) including treatment, country, week, and treatment by week interaction as fixed effects and baseline mAIMS total score as covariate, with an unstructured covariance structure. From the model, the contrast between AFQ056 and placebo at Week 12 was estimated and presented together with a two-sided 90% confidence interval and p-value.

For the secondary efficacy analyses, changes from baseline 2 to Week 12 were analyzed using the MMRM model, similar to the primary efficacy analysis, including treatment, country, week and treatment by week interaction as fixed effects and corresponding baseline total score as covariate, with an unstructured covariance structure. The rating of the Clinician-rated Global Impression of Change (CGIC) on disability due to dyskinesia was analyzed using a Generalized Linear Mixed Model (GLMM) including treatment groups, country, week, treatment by week interaction as fixed effects with cumlogit as link function. From the model, the odds ratio between AFQ056 and placebo at Week 12 was estimated and presented together with a two-sided confidence interval. Comparisons were made between the AFQ056 and placebo groups at the two-sided 10% type I error rate with no adjustment for multiplicity.

All safety analyses were performed on the safety set defined as all patients who received at least one dose of double-blind study drug and had at least one post-baseline safety assessment.

Study Population: Inclusion/Exclusion Criteria and Demographics

Key inclusion criteria:

- Males and females, 30-80 years of age (inclusive)
- Outpatients, residing in the community (nursing home patients are not allowed)
- Clinical diagnosis of Parkinson's disease according to the UK Parkinson's Disease Society Brain Bank Clinical Diagnosis criteria
- Score of ≥ 2 on UPDRS (United Parkinson's Disease Rating Scale) item 32 (i.e. dyskinesia present for greater than 25% of the time) and score of ≥ 2 on UPDRS item 33 (i.e. moderate to severely disabling)
- Onset of dyskinesias at least 3 months before BL1
- On L-dopa for at least 3 years prior to BL1 or, if duration of treatment was ≤ 3 years, then had shown clear responsiveness (UPDRS, part III) to L-dopa treatment
- On a stable treatment regimen with L-dopa and other anti-parkinsonian treatment for at least 4 weeks prior to the first baseline visit (BL1)
- Demonstrated capacity to complete accurate diary ratings

Key exclusion criteria:

- Clinical evidence suggestive of an atypical or secondary form of Parkinson's disease (e.g. Progressive Supranuclear Palsy, Multi Systemic Atrophy)
- History of surgical treatment for PD, including deep brain stimulation
- Score of 5 in the "ON"-state on the Modified Hoehn and Yahr Staging (UPDRS Part V) assessment at Screening
- Any advanced, severe or unstable disease (other than PD) that could interfere with the primary and secondary study outcome evaluations
- Evidence of dementia (or Mini-mental State Examination ≤ 26 at Screening), untreated or ineffectively treated major depressive disorder or currently experiencing hallucinations/psychosis requiring antipsychotic treatment, and/or confusional states
- Treatment prior to first baseline visit (BL1) with any of the following
    - Previous treatment with AFQ056
    - Treatment with strong or moderate inhibitors of CYP3A4
    - Treatment with strong or moderate inducers of CYP3A4
    - Warfarin or digoxin (within 1 week)
    - Centrally acting anti-cholinergic medication (within 1 week)
    - Amantadine (within 2 weeks)
    - Metoclopramide (within 4 weeks)

- Unstable treatment with domperidone, antidepressants, or anxiolytics (within 6 weeks)
- Typical or atypical neuroleptic agents (within 3 months) Duodopa or apomorphine pumps

Participant Flow

Patient disposition – Study completion by treatment (randomized set)

Disposition/Reason	AFQ056 100 mg N=36	Placebo N=25	Total N=61
Completed the study	26 (72.2)	21 (84.0)	47 (77.0)
Discontinued prior to completion of study	10 (27.8)	4 (16.0)	14 (23.0)
Adverse event	10 (27.8)	2 (8.0)	12 (19.7)
Non-compliance with study treatment	0	1 (4.0)	1 (1.6)
Subject/guardian decision	0	1 (4.0)	1 (1.6)

N is the number of patients who entered the double-blind treatment period.

Baseline Characteristics

Demographic summary by treatment group (randomized set)

Demographic variable	AFQ056 100 mg N=36	Placebo N=25	Total N=61
Age (years)			
n	36	25	61
Mean (SD)	65.9 (6.97)	66.6 (7.04)	66.2 (6.95)
Median	65.5	69.0	67.0
Range	49 to 77	50 to 78	49 to 78
Sex, n (%)			
Male	19 (52.8)	15 (60.0)	34 (55.7)
Female	17 (47.2)	10 (40.0)	27 (44.3)
Race, n (%)			
Caucasian	36 (100.0)	25 (100.0)	61 (100.0)
Ethnicity, n (%)			
Hispanic or Latino	8 (22.2)	9 (36.0)	17 (27.9)
Not reported	7 (19.4)	2 (8.0)	9 (14.8)
Unknown	2 (5.6)	2 (8.0)	4 (6.6)
Other	19 (52.8)	12 (48.0)	31 (50.8)
Baseline weight (kg)			
n	36	25	61
Mean (SD)	70.8 (12.08)	71.8 (11.25)	71.2 (11.66)
Median	70.8	75.0	71.5
Range	43.0 to 90.0	50.0 to 89.0	43.0 to 90.0
Baseline height (cm)			
n	36	25	61
Mean (SD)	165.7 (10.51)	168.9 (8.93)	167.0 (9.94)

Demographic variable	AFQ056 100 mg N=36	Placebo N=25	Total N=61
Median	169.0	171.0	170.0
Range	148 to 180	154 to 184	148 to 184
Baseline BMI (kg/m^2)			
n	36	25	61
Mean (SD)	25.9 (4.97)	25.1 (3.39)	25.6 (4.38)
Median	25.4	24.9	25.2
Range	17.9 to 40.6	18.6 to 30.5	17.9 to 40.6
Current smoker, n (%)			
Never	24 (66.7)	19 (76.0)	43 (70.5)
Current	5 (13.9)	3 (12.0)	8 (13.1)
Former	7 (19.4)	3 (12.0)	10 (16.4)

SD=standard deviation, kg=kilogram, cm=centimeter, BMI=Body Mass Index

Disease characteristics by treatment group (randomized set)

	AFQ056 100 mg N=36	Placebo N=25	Total N=61
Age at onset of PD (years) [1]			
n	36	25	61
Mean (SD)	55.4 (10.06)	54.8 (9.65)	55.1 (9.82)
Median	57.0	55.0	57.0
Range	19 to 71	35 to 71	19 to 71
Years since onset of PD symptoms [2]			
n	36	25	61
Mean (SD)	11.89 (6.163)	14.04 (4.730)	12.77 (5.679)
Median	10.00	13.00	12.00
Range	5.0 to 36.0	7.0 to 26.0	5.0 to 36.0
Years since PD diagnosis [2]			
n	36	25	61
Mean (SD)	10.72 (6.008)	11.80 (4.537)	11.16 (5.438)
Median	9.00	12.00	10.00
Range	4.0 to 35.0	4.0 to 20.0	4.0 to 35.0
Years since onset of on-time dyskinesia [2]			
n	36	25	61
Mean (SD)	4.36 (3.424)	4.32 (3.805)	4.34 (3.554)
Median	4.00	3.00	3.00
Range	0.0 to 15.0	0.0 to 16.0	0.0 to 16.0
Years since first initiation of L-dopa [2]			
n	36	25	61
Mean (SD)	8.92 (6.557)	9.88 (5.167)	9.31 (5.999)
Median	7.50	8.00	8.00
Range	1.0 to 34.0	1.0 to 20.0	1.0 to 34.0

[1] Age at onset of PD = (Date of PD diagnosis - birth date +1)/365.25 rounded down to the nearest integer.
[2] Time since event in years is defined as (the screening assessment date - event date + 1)/365.25.

Outcome Measures

Primary Outcome Results

Change from baseline 2 to Week 12 in the mAIMS total score (full analysis set)

					AFQ056 vs. Placebo Difference in LS Mean Change		
Treatment	**n**	**Baseline Mean (SE)**	**Week 12 Mean (SE)**	**Change LS Mean (SE)**	**Mean (SE)**	**90% CI**	**p-value**
AFQ056 100 mg (N=36)	27	12.1 (1.12)	8.8 (1.18)	-3.4 (0.94)	-1.7 (1.31)	(-3.85, 0.53)	0.2095
Placebo (N=25)	22	13.2 (1.04)	10.8 (1.01)	-1.8 (1.03)			

SE = Standard error, CI = confidence interval, LS = least square.
N is the number of FAS patients; n is the number of patients with a value at both baseline and completed week 12 or discontinued after week 8 and had ED visit.
Baseline is the last pre-randomization value.
Least square means, confidence intervals and p-values are derived from MMRM model with treatment group, country, baseline mAIMS total score, visit (in weeks) and treatment*visit interaction as explanatory variables.

Secondary Outcome Results

Change from baseline 2 to Week 12 in the Revised Lang-Fahn ADLDS (Activities of Daily Living Dyskinesia Scale) - patient total score (full analysis set)

					AFQ056 vs. Placebo Difference in LS Mean Change		
Treatment	**n**	**Baseline Mean (SE)**	**Week 12 Mean (SE)**	**Change LS Mean (SE)**	**Mean (SE)**	**90% CI**	**p-value**
AFQ056 100 mg (N=36)	27	13.8 (0.85)	11.4 (0.97)	-2.2 (0.77)	0.1 (1.08)	(-1.73, 1.90)	0.9376
Placebo (N=25)	22	14.2 (0.97)	11.7 (1.09)	-2.2 (0.87)			

N is the number of FAS patients; n is the number of patients with a value at both baseline and completed week 12 or discontinued after week 8 and had ED visit
Baseline is the last pre-randomization value.
Least square means, confidence intervals and p-values are derived from MMRM model with treatment group, country, baseline LFADLDS caregiver total score, visit and treatment*visit interaction as explanatory variables.

Change from baseline 2 to Week 12 in the Revised Lang-Fahn ADLDS - care-giver total score (full analysis set)

					AFQ056 vs. Placebo Difference in LS Mean Change		
Treatment	**n**	**Baseline Mean (SE)**	**Week 12 Mean (SE)**	**Change LS Mean (SE)**	**Mean (SE)**	**90% CI**	**p-value**
AFQ056 100 mg (N=36)	27	14.3 (0.86)	12.1 (0.97)	-2.0 (0.82)	0.4 (1.14)	(-1.54, 2.30)	0.7416
Placebo (N=25)	21	14.2 (0.93)	11.9 (1.12)	-2.3 (0.95)			

N is the number of FAS patients; n is the number of patients with a value at both baseline and completed week 12 or discontinued after week 8 and had ED visit
Baseline is the last pre-randomization value.
Least square means, confidence intervals and p-values are derived from MMRM model with treatment group, country, baseline LFADLDS caregiver total score, visit and treatment*visit interaction as explanatory variables.

CGIC-disability at Week 12 (full analysis set)

	AFQ056 100mg N=36		**Placebo N=25**	
Score	**Total**	**n (%)**	**Total**	**n (%)**
1 - Markedly improved	27	5 (18.5)	21	2 (9.5)
2 - Moderately improved	27	3 (11.1)	21	5 (23.8)
3 - Minimally improved	27	8 (29.6)	21	4 (19.0)
4 - Unchanged	27	8 (29.6)	21	10 (47.6)
5 - Minimally worse	27	2 (7.4)	21	0
6 - Moderately worse	27	1 (3.7)	21	0
7 - Markedly worse	27	0	21	0
Odds Ratio	0.90			
90% CI	(0.20,4.06)			
p-value	0.9119			

N is the number of FAS patients; Total is the number of patients with a value at week 12 or discontinued after week 8 and had ED visit.
CGIC is the Clinical Global Impression of Change scale. p-value is from the generalized linear mixed model with treatment group, country, visit (in weeks) and treatment*visit interaction as explanatory variables, with cumlogit as link function.

Change from baseline 2 to Week 12 in patient diary hours (full analysis set)

					AFQ056 vs. Placebo Difference in LS Mean Change		
Treatment	**n**	**Baseline Mean (SE)**	**Week 12 Mean (SE)**	**Change LS Mean (SE)**	**Mean (SE)**	**90% CI**	**p-value**
Total ON time (hours)							
AFQ056 100 mg (N=36)	26	13.0 (0.42)	13.0 (0.44)	0.0 (0.37)	0.4 (0.54)	(-0.54, 1.27)	0.5055
Placebo (N=25)	20	13.3 (0.74)	12.6 (0.58)	-0.4 (0.45)			
Total OFF time (hours)							
AFQ056 100 mg (N=36)	26	2.4 (0.36)	2.4 (0.34)	-0.1 (0.32)	0.1 (0.47)	(-0.69, 0.88)	0.8372
Placebo (N=25)	20	2.7 (0.56)	2.3 (0.39)	-0.2 (0.40)			
ON time with dyskinesia (hours)							
AFQ056 100 mg (N=36)	26	8.8 (0.55)	7.7 (0.82)	-1.2 (0.75)	0.3 (1.07)	(-1.50, 2.11)	0.7784
Placebo (N=25)	20	9.0 (0.70)	7.8 (0.83)	-1.5 (0.91)			
ON time with troublesome dyskinesia (hours)							
AFQ056 100 mg (N=36)	26	3.4 (0.45)	2.4 (0.59)	-0.9 (0.55)	-0.1 (0.77)	(-1.44, 1.16)	0.8560
Placebo (N=25)	20	4.5 (0.69)	3.3 (0.66)	-0.7 (0.65)			

SE = Standard error, CI = confidence interval, LS = least square.
N is the number of FAS patients; n is the number of patients with a value at both baseline and completed week 12 or discontinued after week 8 and had ED visit
Baseline is the last pre-randomization value.
Least square means, confidence intervals and p-values are derived from MMRM model with treatment group, country, baseline patient diary hours, visit and treatment*visit interaction as explanatory variables.

Change from baseline 2 to Week 12 in the UPDRS part III total score (full analysis set)

					AFQ056 vs. Placebo Difference in LS Mean Change		
Treatment	**n**	**Baseline Mean (SE)**	**Week 12 Mean (SE)**	**Change LS Mean (SE)**	**Mean (SE)**	**90% CI**	**p-value**
AFQ056 100 mg (N=36)	27	22.3 (2.21)	18.1 (1.50)	-3.6 (1.27)	-0.5 (1.77)	(-3.50, 2.45)	0.7677
Placebo (N=25)	22	20.9 (1.39)	18.8 (1.65)	-3.1 (1.46)			

SE = Standard error, CI = confidence interval, LS = least square.
N is the number of FAS patients; n is the number of patients with a value at both baseline and completed week 12 or discontinued after week 8 and had ED visit
Baseline is the last pre-randomization value.
Least square means, confidence intervals and p-values are derived from MMRM model with treatment group, country, baseline UPDRS part III total score, visit and treatment*visit interaction as explanatory variables.

Change from baseline 2 to Week 12 in items 32, 33 and 34 of the UPDRS part IV (full analysis set)

					AFQ056 vs. Placebo Difference in LS Mean Change		
Treatment	**n**	**Baseline Mean (SE)**	**Week 12 Mean (SE)**	**Change LS Mean (SE)**	**Mean (SE)**	**90% CI**	**p-value**
UPDRS, item 32 (Duration of dyskinesia)							
AFQ056 100 mg (N=36)	27	2.5 (0.14)	2.3 (0.18)	-0.2 (0.16)	0.3 (0.22)	(-0.06, 0.69)	0.1612
Placebo (N=25)	22	2.7 (0.15)	2.1 (0.20)	-0.5 (0.18)			
UPDRS, item 33 (Disability due to dyskinesia)							
AFQ056 100 mg (N=36)	27	2.0 (0.11)	1.6 (0.17)	-0.5 (0.17)	0.1 (0.24)	(-0.29, 0.52)	0.6440
Placebo (N=25)	22	2.3 (0.12)	1.6 (0.19)	-0.6 (0.19)			
UPDRS, item 34 (Painful dyskinesia)							
AFQ056 100 mg (N=36)	27	0.7 (0.16)	0.4 (0.12)	-0.4 (0.12)	0.0 (0.17)	(-0.29, 0.29)	0.9847
Placebo (N=25)	22	1.0 (0.24)	0.5 (0.22)	-0.4 (0.14)			

SE = Standard error, CI = confidence interval, LS = least square.
N is the number of FAS patients; n is the number of patients with a value at both baseline and completed week 12 or discontinued after week 8 and had ED visit
Baseline is the last pre-randomization value.
Least square means, confidence intervals and p-values are derived from MMRM model with treatment group, country, corresponding baseline score, visit and treatment*visit interaction as explanatory variables.

Safety Results

Number (%) of patients with treatment emergent adverse events (AEs) by primary system organ class (safety set)

Primary SOC (System Organ Class)	**AFQ056 100 mg N = 36 n (%)**	**Placebo N = 25 n (%)**	**Total N = 61 n (%)**
Number of patients with at least one AE	28 (77.8)	12 (48.0)	40 (65.6)
Nervous system disorders	12 (33.3)	6 (24.0)	18 (29.5)
Psychiatric disorders	12 (33.3)	0	12 (19.7)
Gastrointestinal disorders	6 (16.7)	2 (8.0)	8 (13.1)
Musculoskeletal and connective tissue disorders	5 (13.9)	3 (12.0)	8 (13.1)
General disorders and administration site conditions	4 (11.1)	3 (12.0)	7 (11.5)
Injury, poisoning and procedural complications	4 (11.1)	3 (12.0)	7 (11.5)
Eye disorders	3 (8.3)	0	3 (4.9)
Infections and infestations	3 (8.3)	2(8.0)	5 (8.2)
Investigations	3 (8.3)	0	3 (4.9)
Metabolism and nutrition disorders	3 (8.3)	0	3 (4.9)
Renal and urinary disorders	3 (8.3)	1 (4.0)	4 (6.6)
Vascular disorders	3 (8.3)	1 (4.0)	4 (6.6)

Primary SOC (System Organ Class)	AFQ056 100 mg N = 36 n (%)	Placebo N = 25 n (%)	Total N = 61 n (%)
Skin and subcutaneous tissue disorders	2 (5.6)	0	2 (3.3)
Ear and labyrinth disorders	1 (2.8)	0	1 (1.6)
Respiratory, thoracic and mediastinal disorders	1 (2.8)	1 (4.0)	2 (3.3)
Reproductive system and breast disorders	0	1 (4.0)	1 (1.6)

Note: Primary SOCs are presented in descending order in the AFQ056 treatment group.
- A patient with multiple occurrences of an AE under one treatment is counted only once in the AE category for that treatment.
- A patient with multiple adverse events within a primary SOC is counted only once.
- MedDRA (Medical Dictionary for Regulatory Activities Version 15.0 has been used for the reporting of adverse events.

Most frequently reported (preferred term > 5% in any treatment group) treatment emergent adverse events by preferred term (safety set)

Preferred term	AFQ056 100 mg N=36	Placebo N=25	Total N=61
Number of patients with at least one AE	28 (77.8)	12 (48.0)	40 (65.6)
Dizziness	4 (11.1)	0	4 (6.6)
Hallucination, visual	4 (11.1)	0	4 (6.6)
Dyskinesia	3 (8.3)	3 (12.0)	6 (9.8)
Headache	3 (8.3)	1 (4.0)	4 (6.6)
Akinesia	2 (5.6)	2 (8.0)	4 (6.6)
Anxiety	2 (5.6)	0	2 (3.3)
Back pain	2 (5.6)	1 (4.0)	3 (4.9)
Confusional state	2 (5.6)	0	2 (3.3)
Constipation	2 (5.6)	0	2 (3.3)
Fall	2 (5.6)	2 (8.0)	4 (6.6)
Haemoglobin decreased	2 (5.6)	0	2 (3.3)
Insomnia	2 (5.6)	0	2 (3.3)
Muscle spasms	2 (5.6)	0	2 (3.3)
Nasopharyngitis	2 (5.6)	0	2 (3.3)
Nausea	2 (5.6)	1 (4.0)	3 (4.9)
Oedema peripheral	2 (5.6)	0	2 (3.3)
Orthostatic hypotension	2 (5.6)	0	2 (3.3)
Parkinsonian gait	2 (5.6)	0	2 (3.3)
Vision blurred	2 (5.6)	0	2 (3.3)
Asthenia	1 (2.8)	2 (8.0)	3 (4.9)

- Note: Preferred terms are sorted in descending frequency by AFQ056 100 mg column.
- A patient with multiple occurrences of an AE under one treatment is counted only once in the AE category for that treatment.
- MedDRA Version 15.0 has been used for the reporting of adverse events.

Overall summary of adverse events– n (%) of patients (safety set)

	AFQ056 100 mg N = 36 n (%)	Placebo N = 25 n (%)	Total N = 61 n (%)
Patients with at least one TEAE (treatment emergent adverse event)	28 (77.8)	12 (48.0)	40 (65.6)
Patients with at least one serious adverse event (SAE)	4 (11.1)*	0	4 (6.6)
Patients who died	0	0	0
Patients who discontinued from study due to AEs	10 (27.8)	2 (8.0)	12 (19.7)
Discontinued from study due to SAEs	3 (8.3)	0	3 (4.9)
Discontinued from study due to non-serious AEs	7 (19.4)	2 (8.0)	9 (14.8)

Note: - A patient with multiple occurrences of an AE under one treatment is counted only once in the AE category for that treatment.
* paralytic ileus/inguinal hernia, worsening gait/peripheral edema, visual hallucination/hallucination and worsening of Parkinson's disease/suicidal ideation
- MedDRA Version 15.0 has been used for the reporting of adverse events.

Date of Clinical Trial Report

CSR published: 19 August 2013

Date Inclusion on Novartis Clinical Trial Results Database

10 September 2013

Date of Latest Update