

LATE-BREAKING ABSTRACTS



International Parkinson and
Movement Disorder Society
Pan American Section

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Special Meeting Theme:
Therapeutics of Movement
Disorders in the Americas



#pascongress

LBA 1

Restless Limbs Syndrome (RLS): Natural History vs. Augmentation

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Objective: To determine the incidence of augmentation in a large clinical population with RLS and to compare its manifestations with the natural history of RLS in an untreated population.

Background: The natural history of RLS is not well-defined. Treatment with Dopamine Agonists (DA) can have side effects including augmentation which can cause symptoms to worsen, occur earlier in the day, and spread to involve other regions of the body. The precise incidence of augmentation is unknown but must be considered in relation to the natural history of RLS itself.

Methods: In this retrospective, population-based study 983 patients with RLS completed a survey addressing location and diurnal variation of symptoms at onset (mean age= 38 yrs) and presentation (mean age=53 yrs). 772 patients received DAs (M group) and 102 did not (NM group). The groups were compared for progression.

Results: M and NM groups were matched at onset for age, gender, leg onset (58.8% vs. 57.8%) and nocturnal symptoms (46.3% vs. 52.7%). By the time the questionnaire was administered ("presentation") symptoms involved the arms in 56.2% M and 49.5% NM ($p=0.68$). Symptoms became diurnal in 74% M and 73.4% NM ($p=0.50$). 120 of 772 treated patients (15.5%) experienced worsening of symptoms or side effects. 36 described changes suggesting augmentation such as: worsening of pain/symptoms (22), earlier onset (5) or shorter effects of medication (9).

Conclusions: These data support that the natural history of RLS is that of a progressive disease including spread of symptoms over time and space. This progression was not significantly different between medicated and non-medicated groups.

LBA 2

Comparison of GBA K198E Mutation Prevalence in Colombian and Hispanic Populations

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Objective: In order to address the paucity of Parkinson's disease (PD) genetic studies in Latin America, we aimed to confirm a previous report of GBA K198E prevalence among Colombians with PD and to compare with that of an American Hispanic cohort.

Background: Mutations within the GBA gene are classically associated with Gaucher's disease, a childhood lysosomal storage disorder, but also with early onset PD and patients have a higher incidence of cognitive decline. GBA pathogenic variants have been identified in 5-10% of individuals with PD and are the strongest risk factor for PD. Mutation frequencies vary between populations and a recent study found a GBA mutation in 10% of Colombian patients with PD. The majority of these patients carried the K198E mutation, which is far less prevalent in previous reports of other more diverse populations with relatively low Latin America representation.

Methods: We performed genetic screening on samples from 200 Colombians (Controls = 58, PD = 142) and 67 Hispanics with PD. Screening consisted of Sanger sequencing of the GBA K198E missense mutation.

Results: We identified the K198E mutation in Colombians with PD (n = 3, 2.1%) and controls (n = 1, 1.7%). This mutation was not present in our American Hispanic cohort.

Conclusions: Our findings add to the relatively sparse amount of information regarding PD genetics in Latin America. Our cohort of Colombians was larger than a previously described cohort of Colombians with PD that showed K198E prevalence three times higher than ours. This suggests that there may be substantial heterogeneity of contributing heritages and underscores the need for more large scale genetic studies in Latin America in order to increase our understanding of PD clinical heterogeneity and pathomechanisms.

LBA 3

Identification of Known Genes in Colombian and Ecuadorian Parkinson's Disease Patients

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Objective: Our objective was to address the relatively small number of genetic studies of Parkinson's disease (PD) in Latin American populations by performing genetic screens on cohorts of patients with PD from Colombia and Ecuador.

Background: PD is a complex neurodegenerative disease characterized by loss of dopaminergic cells in the substantia nigra due to abnormal accumulation of alpha synuclein. Despite this knowledge, our understanding of PD pathomechanisms remains incomplete. Genetic studies continue to contribute to this growing body of knowledge; however, these studies are overrepresented by patients from the United States, Europe, and Asia. Performing genetic analyses of underrepresented populations, including Latin America, will likely add to our knowledge regarding the genetic underpinnings of PD.

Methods: We performed genetic screening on samples from 85 Colombians (Controls = 25, Late Onset PD = 29, Early Onset PD = 26, additional samples from independent families = 5) and 426 Ecuadorians with PD (Late Onset PD = 355, Early Onset = 71). Screening consisted of Sanger sequencing of common PD-related variants within SCNA, LRRK2, PARKIN, PINK1, DJ-1 and single nucleotide polymorphism(SNP) assays for GBA, VPS35, ApoE and MAPT. Multiplex Ligation-dependent Probe Amplification (MLPA) was performed on early onset PD (EOPD) samples to identify gene dosage effects.

Results: We identified variants in PARKIN, PINK1, and LRRK2 within our cohort of Colombians with PD. MLPA Colombian EOPD samples revealed homozygous duplications of PARKIN exon 7 in one patient as well as exons 5 & 6 in a set of two siblings, whose parents both had heterozygous duplications. Among PD patients from Ecuador, SNPs were identified within LRRK2, ApoE, MAPT, and GBA.

Conclusions: Our findings add to the sparse amount of information regarding the prevalence of common PD genetic variants in Latin America and illustrate the continued importance of single family studies, which allow for the detection of novel genetic modifications. We expect this to lead to a more thorough understanding of the clinical heterogeneity of PD as well as pathomechanisms underlying this devastating disease.

LBA 4

Apomorphine Infusion for Advanced Parkinson's Disease: A Phase III, Long-Term, Openlabel Study

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Objective: Investigate the safety and efficacy of apomorphine (APO) infusion in Parkinson's disease (PD) patients inadequately controlled with levodopa and additional PD therapies.

Background: Although APO infusion has been used internationally for >25 years, safety and efficacy data are absent in the US.

Methods: This was an open-label, long-term outpatient study of APO infusion at 18 US PD clinics (NCT02339064). PD patients with inadequate motor control despite optimized treatment with levodopa and an additional PD therapy were eligible for the study (≥ 3 hours of daily OFF time). Patients were titrated to individualized APO doses to reach best waking day efficacy without intolerable adverse effects (AEs). Once the optimal infusion dose was identified, patients entered a 52-week open-label maintenance period.

Results: Of the 99 patients enrolled, 85 were initiated, 69 completed 12 weeks maintenance therapy and 46 completed 52 weeks. The main reason for discontinuation was AEs, mostly in the dose titration phase (17 of the 29 withdrawals due to AE occurred during titration). The mean \pm SD daily APO maintenance dose was 45.6 \pm 23.0 mg (3.4mg/h). APO infusion was generally well-tolerated and no unexpected safety signals were observed. All patients had ≥ 1 AE, the most common treatment-related AEs were infusion site nodules (77.8%) and dyskinesia (38.4%, predominantly in titration phase). Daily OFF time was reduced from 6.6 \pm 2.4 h at baseline to 3.5 \pm 2.7 h (reduction of 3.0 \pm 3.2 h) at Week 12 (primary efficacy endpoint), a magnitude sustained until Week 52. Mean \pm SD ON time without troublesome dyskinesia increased from 9.3 \pm 2.6 h at Baseline to 12.6 \pm 2.8 hours at Week 12 and 13.1 \pm 2.3 hours at Week 52. Patient Global Impression – Change (PGI-C) improved at Week 12, with 89 patients (89.9%) reporting improvement. The Parkinson's Disease Questionnaire (PDQ-39) total scores were reduced by -4.5 \pm 10.6 points at Week 12 and -3.0 \pm 11.4 points at Week 52.

Conclusions: In this open-label Phase III study, subcutaneous apomorphine infusion was generally safe and effective for up to one year in patients with PD and advanced motor fluctuations.

LBA 5

Discrepancy of the Distribution of Alpha-Synuclein Oligomers and Lewy Bodies in Parkinson's Disease Brain

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Objective: To examine the distribution of alpha-synuclein (α SYN) oligomers in Parkinson's disease (PD) and compare the distribution of α SYN oligomers and Lewy bodies (LBs).

Background: LBs are the late-stage aggregations of α SYN and have been considered as the pathological hallmark of PD. The staging system of Braak, which is based on the distribution of LBs, has been widely used. However, due to the presence of incidental LBs in elderly individuals without Parkinsonism and the absence of LBs in some of the familial PD patients, LBs cannot fully explain the pathogenesis of PD.

Methods: We examined 5 Parkinson's disease (PD) patients and 9 control cases. We conducted phosphorylated- α SYN immunostaining to detect LBs and adopted a proximity ligation assay (PLA) to examine the distribution of α SYN oligomers.

Results: As well as the punctate staining in remaining neurons in the substantia nigra, PD patients showed widespread α SYN-PLA signals in the putamen, pontine nuclei, and the frontal cortex, whereas such signals were rarely found in control cases. Among PD patients, the Braak stage was 3 in 2 patients, 5 in 1 patient, and 6 in 2 patients. LBs themselves were not stained in α SYN-PLA staining and the punctate signal of α SYN-PLA was found in the periphery of LBs. We found punctate staining of α SYN oligomers in cortical neurons in patients with Braak stage 3, as well as in those patients with Braak stage 5 and 6. The distribution of α SYN oligomers was more widespread than that of LBs.

Conclusions: We visualized α SYN oligomers using a PLA approach and found a widespread distribution of α SYN oligomers in cortical neurons of PD. The formation of α SYN oligomers may precede the formation of LBs and α SYN oligomers may distribute widely throughout the brain even in the earlier course of PD.

LBA 6

Sex-Based Differences in the Activation of Peripheral Blood Monocytes in Early Parkinson's Disease

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Objective: Determine whether there is evidence for activation of peripheral blood monocytes in early Parkinson disease.

Background: Increasing evidence points to a role of neuro-inflammation in the etiology and progression of Parkinson's disease (PD). Monocytes are a key component of the innate immune system. In animal models of PD, monocytic activation is an early event and is required in order to establish a degenerative phenotype. Monocyte activation has not previously been directly examined in early, untreated human PD.

Methods: Patients with early PD (UK Brain Bank criteria) within 2 years of symptom onset and not taking any anti-parkinsonian medication along with age-matched control subjects were recruited. A total of 21 male (10 control, 11 PD) and 13 female (6 control, 7 PD) subjects were enrolled. Monocytes were isolated from fresh blood using a negative selection method. Monocyte populations were analyzed by flow cytometry. Monocyte gene expression was examined using RNA-seq, and used to characterize states of monocyte activation through Gene Set Enrichment Analysis (GSEA). Patterns of gene expression were compared using the approach of Xue et al. (*Immunity*. 2014 Feb 20; 40(2): 274–288) to a series of reference states representing differential activation of monocytes.

Results: Principal component analysis was used to examine the unbiased grouping of PD and control samples utilizing the 100 most variable genes. This revealed a very strong effect of sex. Separation of the data by sex demonstrated that in the females, there was clear separation by PD vs. control, while the gene expression data in the males was more heterogeneous. A sexually dimorphic response to PD was also seen in flow cytometry analysis, with increased non-classical (CD16+) monocytes in females, and increased intermediate monocytes (CD14+CD16+) in males. GSEA was performed in monocytes from males and females separately (Figure 1). In the females, we detected enrichment of 8 different gene modules; two of these were highly significant (Modules 7 and 8, FDR q-value <.001). Both of these models are classical "M1" pro-inflammatory gene programs, and strongly associated with response to interferon-gamma. In the males, none of the gene models achieved statistical significance.

Conclusions: This study demonstrates clear sex-based differences in monocyte activation in early PD. In females, there is strong activation of blood monocytes with polarization towards an "M1" phenotype. Monocytes of this kind are typically associated with pro-inflammatory actions that may lead to tissue injury. In contrast, we did not observe any statistically significant change in gene expression patterns in males with early PD. One potential explanation for this difference is that there may be increased heterogeneity in the males; we did have a larger sample size for males, but if there are subgroups with different states of inflammatory activation in males, our sample may still be insufficient. These data are in line with clinical observations which suggest difference in the incidence, presentation, and progression of PD in men and women. They also point to the critical importance of inclusive enrollment of both sexes in studies of PD, and the need to consider that there may be sex-based differences in the underlying mechanism of the disease.

Macrophage Stimulation Module Enrichment
(Xue et al., Immunity, 2014)

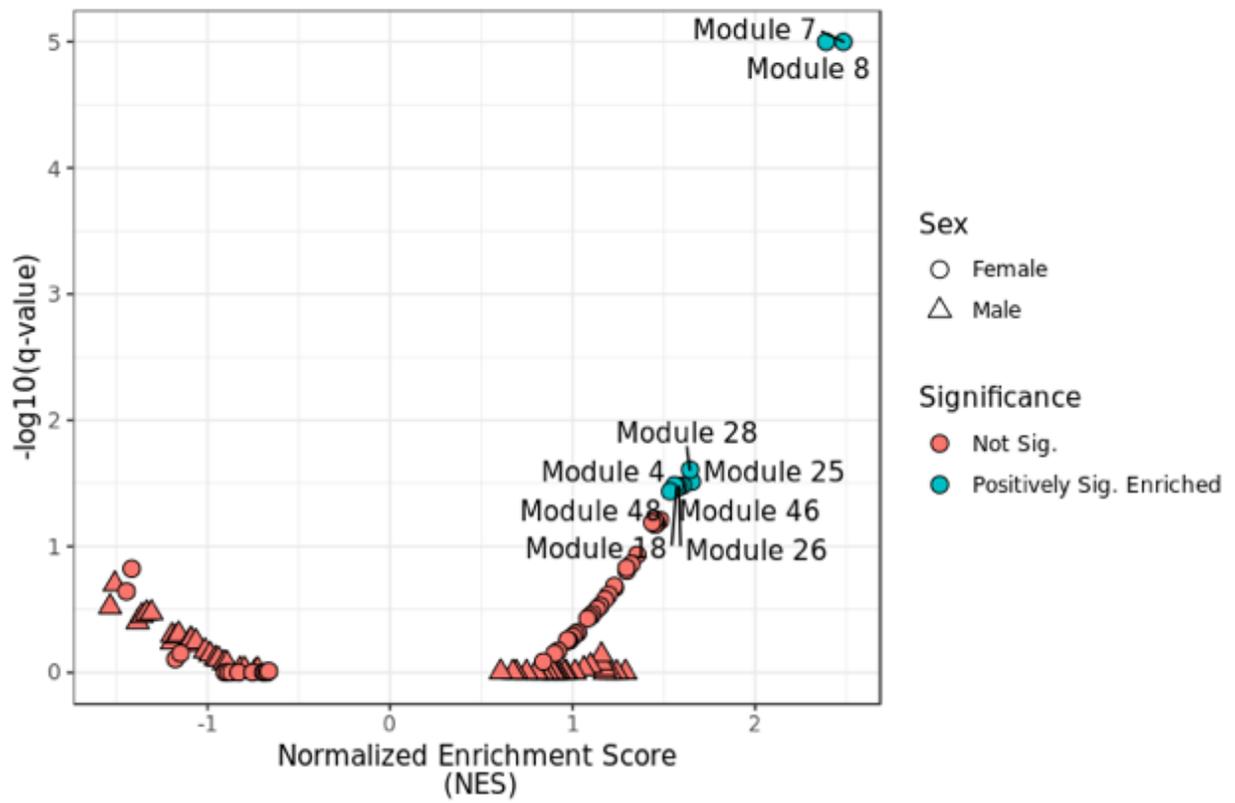


Figure 1

LBA 7

Synergistic Anti-Dyskinetic Effects of Pridopidine and Amantadine in the 6-OHDA Lesioned Rat Model of Parkinson's Disease

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Objective: To assess the effect of pridopidine alone, and in combination with amantadine (AMT) on established L-DOPA-induced abnormal involuntary movements (AIMs) in the 6-OHDA-lesioned rat model of Parkinson's disease (PD).

Background: The anti-dyskinetic effect of pridopidine is demonstrated in the MPTP-macaque model for levodopa-induced dyskinesia (LID). Pridopidine produces a dose dependent significant and meaningful decrease in LID without compromising the anti-parkinsonian benefit of L-DOPA. The ability of pridopidine to reduce LID in PD patients is currently assessed in a double-blind phase 2 clinical trial (ClinicalTrials.gov Identifier: NCT03922711). AMT represents "standard-of-care" for LID in PD patients (PD-LID). However, the therapeutic utility of AMT is often limited by adverse events such as hallucinations, sedation, cognitive problems and poor tolerance in 40-50% of patients. As the anti-dyskinetic actions of pridopidine and AMT involve distinct mechanisms, we hypothesize that their combination may have a synergistic or additive anti-dyskinetic benefit. Combination of pridopidine and AMT at sub-optimal doses can potentially enhance the efficacy of each drug given separately, while reducing side effects.

Methods: Female Sprague-Dawley rats were rendered hemi-parkinsonian with 6-OHDA. Stable and reproducible AIMs were established by repeated L-DOPA administration over a period of 3 weeks. The effects of acute administration of treatments were then assessed in combination with L-DOPA (6 mg/kg). The order of treatments within each animal was randomised using an incomplete Latin Square-type design. AIMs were assessed every 20 min for a period of 3 h following L-DOPA administration.

Results: Pridopidine doses of 3, 15, 30 and 60 mg/kg were administered to L-DOPA treated 6-OHDA rats in order to determine the effect on L-DOPA-induced AIMs as monotherapy. Pridopidine doses of 30 and 60 mg/kg significantly reduce AIMs by 21% and 42%. By contrast, lower doses of 3 and 15 mg/kg show no effect. Thus, pridopidine 15 mg/kg was chosen as the suboptimal dose to be tested in combination with AMT. AMT effects on AIMs were previously determined by us to be suboptimal at 5 (no effect) and 10 mg/kg (mild but non-significant effect). At the chosen suboptimal doses, neither pridopidine nor AMT affect levels of AIMs. However, in combination we observe a significant reduction in levels of AIMs. AMT-pridopidine combination shows a significant reduction in AIMs during the 'peak-effect' period (20-120 min) (36%, * $p < 0.05$ and 63%, * $p < 0.01$ for AMT 5 and 10 mg/kg respectively).

Conclusions: We demonstrate a synergistic anti-dyskinetic effect of pridopidine and AMT in the 6-OHDA lesioned rat model of Parkinson's disease. These data further support the potential of pridopidine as a therapeutic for LID and suggest that low-dose combination of pridopidine and AMT may be beneficial in dyskinetic PD patients, reducing the known side effects associated with AMT treatment while optimising the anti-dyskinetic effect.

LBA 8

Phase 2a Open-Label Study to Evaluate the Safety, Tolerability and Efficacy of CAD-1883 in Essential Tremor (Cadence-1)

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Objective: To assess the safety, tolerability and efficacy of CAD-1883 in patients with essential tremor (ET).

Background: CAD-1883 is a novel, first-in-class, positive allosteric modulator of small conductance calcium-activated potassium (SK) channels. Positive modulation of SK channels decreases Purkinje cell firing frequency by increasing the duration of afterhyperpolarization. CAD-1883 significantly reduced tremor in the rat harmaline-induced tremor model at exposures readily achieved in a Phase 1 study that evaluated dosages up to 600 mg twice daily for 14 days.

Methods: Two cohorts of subjects were enrolled with a ≥ 3 -year history of essential tremor (ET) and an Essential Tremor Rating Assessment Scale performance score (TETRAS-PS) ≥ 15 points based on centralized video ratings. CAD-1883 300 mg twice daily was administered for 14 days for all subjects. The dosing interval was shortened between Cohort 1 and 2 to increase exposure. Clinical assessments, including centralized blinded video reviews of TETRAS-PS, which was blinded to study visit, and a wearable sensor (Kinesia One), occurred during screening, baseline, and days 1, 7, 14 and 21.

Results: Cohorts 1 and 2 enrolled 18 and 7 subjects respectively. No SAEs were reported. One subject discontinued due to an AE (jittery, tachycardic). Fatigue and lethargy were reported in two subjects. Centrally rated, blinded, TETRAS-PS ratings at Day 14 improved by 2.8 (SD=3.6) for Cohort 1 and 3.8 (SD=7.4) for Cohort 2. Improvement of ≥ 5 points in TETRAS-PS was observed in 41% of subjects. Centralized TETRAS-PS assessments correlated with Kinesia One. The modified dosing schedule in Cohort 2 increased mean exposure by approximately 70% compared to Cohort 1.

Conclusions: CAD-1883 was well tolerated in this Phase 2a study. An increase in mean exposure coincided with a larger improvement in the TETRAS-PS score for Cohort 2 compared to Cohort 1. A larger, controlled study is warranted to confirm this efficacy signal.

LBA 9

Improvement in UPDRS Motor Scores after CVT-301 Treatment is Associated with Improved Scores in the Parkinson's Disease Questionnaire Activities of Daily Living

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Objective: Post hoc analysis to evaluate activities of daily living (ADL) changes as assessed by Parkinson's Disease Questionnaire (PDQ-39) ADL subdomain scores and correlations with changes in the Unified Parkinson's Disease Rating Scale Part III (UPDRS-III) over the 12-week period of a phase 3 study[1].

Background: In the SPAN-PD study, CVT-301 84mg significantly improved motor function in patients experiencing OFF periods at week 12, as measured by lower UPDRS-III scores, 30 minutes postdose ($P=0.009$), and 58% of patients achieved and maintained an ON state <60 minutes postdose vs 36% on placebo ($P=0.003$). 71.4% of patients on CVT-301 84mg reported improvement in Patient Global Impression of Change (PGIC) vs 46.4% on placebo (nominal $P<0.001$)[1]. A post hoc analysis showed PDQ-39 ADL subdomain scores correlated with PGIC scores: as PDQ-39 ADL scores decreased (improved), PGIC was more positive. A PDQ-39 ADL mean change of -1.98 units was associated with PGIC outcomes of "a little improvement." Also, the lower the PDQ-39 ADL score, the more positive the perception of improvement. Although not statistically significant, the PDQ-39 ADL treatment difference (84mg vs placebo) of -2.08 surpassed the desired threshold of -1.98 units[2].

Methods: PD patients experiencing OFF periods on an oral carbidopa/levodopa regimen were randomized to placebo or CVT-301 60mg or 84mg for the treatment of OFF period symptoms as needed up to 5 times/day. PDQ-39 and UPDRS-III were completed at baseline and 4, 8, and 12 weeks.

Results: Week 12 UPDRS-III improvements 30 minutes postdose were associated with a -3.43 point mean improvement in PDQ-39 ADL subdomain score, exceeding the -1.98 threshold. Conversely, worsening (or no change) in UPDRS-III scores at 30 minutes postdose was associated with a $+1.33$ worsening PDQ-39 ADL scores. A $\geq 30\%$ UPDRS-III improvement, was associated with a -4.42 point improvement in PDQ-39 ADL scores. Responder ON patients showed greater improvements in PDQ-39 ADL (-4.05) than nonresponders (-0.82).

Conclusions: Post hoc analyses showed that UPDRS-III improvements and responder ON status were associated with improvements in PDQ-39 ADL scores.

References: [1] LeWitt PA, Hauser RA, Pahwa R, et al. Safety and efficacy of CVT-301 (levodopa inhalation powder) on motor function during off periods in patients with Parkinson's disease: a randomised, double-blind, placebo-controlled phase 3 trial. *Lancet Neurol.* 2019;18(2):145-154. [2] LeWitt PA, Hauser RA, Oh C, et al. Inhaled levodopa (CVT-301) for treatment of OFF periods in Parkinson's disease: efficacy as assessed by 39-item Parkinson's disease quality of life questionnaire [abstract/poster P23.10]. World Parkinson Congress: Kyoto, Japan, 4–7 June 2019. *J Parkinsons Dis.* 2019;9(S1):157. <https://content.iospress.com/articles/journal-of-parkinsons-disease/jpd199900>.

LBA 10

Improvement in SAPS-PD Assessment Over 10 Weeks of Pimavanserin Treatment for Parkinson's Disease Psychosis

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Objective: In a prespecified prospective analysis, we evaluated the efficacy and tolerability of pimavanserin in patients who either continued treatment with 34 mg pimavanserin for 10 weeks (i.e., randomized to pimavanserin arm in double-blind, placebo-controlled studies or previous extension studies) or began treatment with 34 mg pimavanserin (i.e., had been randomized to placebo in double-blind, placebo-controlled study) for 4 weeks.

Background: Parkinson's disease psychosis (PDP) is a common nonmotor symptom that affects up to 60% of patients with PD. Pimavanserin, a selective 5-HT_{2A} inverse agonist/antagonist without D₂ affinity, demonstrated efficacy for PDP in randomized, placebo-controlled study.

Methods: Patients completing a 6-week placebo-controlled Core Study could enroll in a 4-week open-label extension (OLE) and receive pimavanserin 34 mg once daily. In the OLE, all patients remained blinded to previous treatment and underwent assessments at Week 4 with the Scale for the Assessment of Positive Symptoms (SAPS) PD and H+D scales, Clinical Global Impression (CGI) Improvement and Severity scales, Caregiver Burden Scale (CBS), and adverse events.

Results: Of 199 patients entering the Core Study, 171 entered the OLE, and 148 (87%) completed Week 4. Among patients who received placebo in the Core Study, mean (SD) change from OLE baseline to OLE Week 4 for the SAPS-PD was -3.4 (6.3); $p < 0.0001$ (Figure). Mean change from Core Study baseline to OLE Week 4 for SAPS-PD was similar among prior pimavanserin 34 mg and prior placebo-treated participants (-6.7 vs. -6.3). A similar pattern of improvement was observed with CGI-I, CGI-S (Figure), CBS, and SAPS-H+D in patients previously treated with placebo. Adverse events were reported by 91 (53.2%) patients during the OLE.

Conclusions: The beneficial effects observed with pimavanserin in the Core Study were maintained for an additional 4 weeks. Improvements at OLE Week 4 were similar in patients who received placebo and pimavanserin in the Core Study. Results support the efficacy and durability of response with pimavanserin 34 mg for PDP.

Figure 1. LS mean (SE) change from baseline for SAPS-PD score

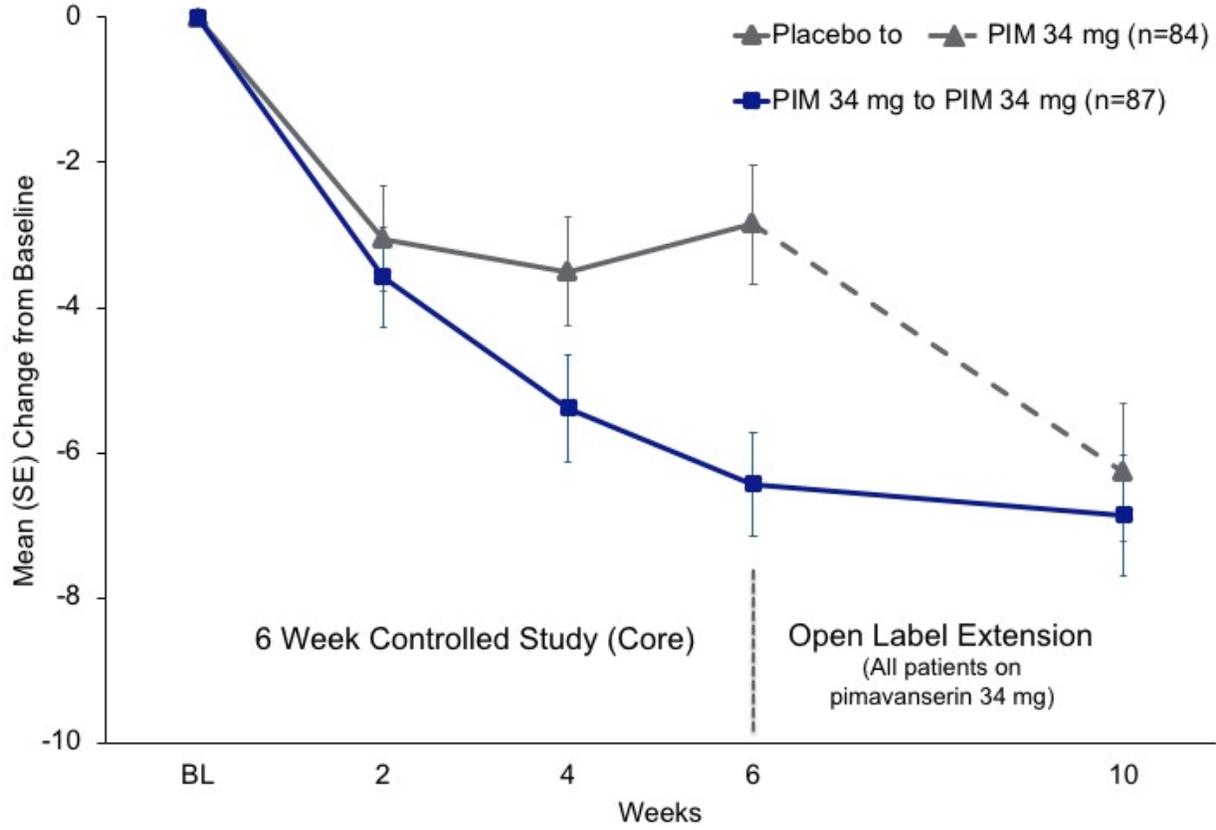


Figure 1

LBA 11

Restless Legs Syndrome/Willis-Ekbom Disease in Obstructive Sleep Apnea: Prevalence and Association Factors Among Southern Brazilians

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Objective: The main study aim was to estimate RLS prevalence and severity and its association factors in a sample of adult OSA individuals.

Background: Very few studies had evaluated restless legs syndrome/Willis-Ekbom disease (RLS) prevalence among obstructive sleep apnea (OSA) patients. This comorbidity prevalence, its severity and association factors were not well addressed in those studies after recent modification in diagnostic criteria.

Methods: Prospective, cross-sectional study including 490 Brazilian OSA patients, evaluated by full-night polysomnography. RLS diagnosis was established by structured face-to-face interview when 2014 International Restless Legs Syndrome Study Group (IRLSSG) criteria were fulfilled and after mimics exclusion. OSA was diagnosed by International Classification of Sleep Disorders criteria.

Results: Prevalence of RLS was 18.6% by IRLSSG diagnostic criteria and mimics exclusion or 11.2% by additional frequency criteria (≥ 3 /week). Less than 15% RLS individuals was aware of diagnosis before the study. Mean IRLSSG severity score was 17.0 ± 6.8 . RLS predominated among women. Excessive daytime sleepiness was similar in RLS and non-RLS individuals. Chronic insomnia symptoms, mainly sleep-onset difficulty, were more prevalent in RLS group. Anxiety and depression scale scores were higher among RLS patients and they were associated to RLS severity. Mild OSA was positively associated to RLS and there was a negative association between severe OSA and RLS.

Conclusions: Despite being a relatively prevalent condition among OSA patients, RLS was largely under recognized in this sample. RLS severity was correlated to higher scores in both anxiety and depression scales. In multinomial logistic regression, chronic insomnia symptoms were the main RLS association factor. On the other hand, obesity was negatively associated to RLS diagnosis among OSA individuals.

LBA 12

Assessing Head Tremor Severity in Cervical Dystonia with Videorecordings and Computer Vision

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Objective: The objective of this study was to test the validity of computer vision-based methods for measuring severity of head tremor (HT) in cervical dystonia (CD).

Background: Quantifying HT severity is critical for research into the pathophysiology of CD and as an outcome measure for clinical trials. The most widely used approach is clinical rating scales, such as the “tremor” item on the Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS). However, clinical rating scales are based on human judgement, which is inherently subjective. In contrast, computational analyses of video recordings that capture head orientation offer the possibility of measuring HT severity objectively.

Methods: We analyzed digital videos from a cohort of 206 patients with isolated CD originally recruited from 10 sites in North America through the Dystonia Coalition's project to validate the Comprehensive Cervical Dystonia Rating Scale. The videos were recorded at a rate of 30 frames per second while patients were instructed to let their head drift to its most natural dystonic position. Using the Computational Motor Objective Rater (“CMOR”) software, we quantified HT based on the spectral power at the peak frequency of their head rotation angle. HT was also quantified clinically using a global severity scale of 0-10. We tested the convergent validity between CMOR and the clinical ratings with Spearman's correlation.

Results: We removed cases with videographer and/or patient protocol non-compliance (e.g. videographer visible in video, video not recorded with a tripod, etc., N = 49), leaving N = 157 patients for subsequent analysis. The patients spanned the range of 0-9 on the clinical rating of HT. CMOR's HT rating was positively correlated with the clinical HT rating (Spearman's rho = 0.58, p < 0.001).

Conclusions: This study demonstrates that computational video analysis can capture the severity of HT associated with CD. Thus, it could form the basis for objective assessment that is complementary to rating scales yet amenable to widespread use in the clinical setting, thereby reducing measurement noise for assessing HT severity in CD.