

Impact of patient recruitment before and during COVID shelter-in-place: What do unblinded data reveal

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Disclosures

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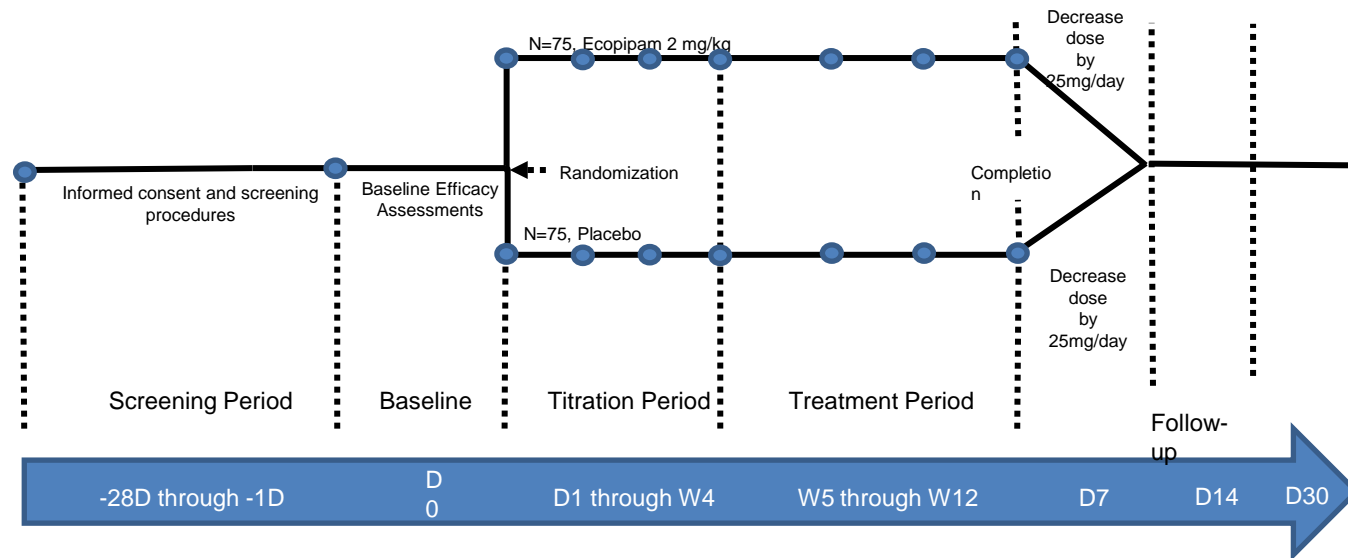
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EBS-101-CL-001

A Multicenter, Placebo-Controlled, Double-Blind, Randomized, Parallel-Group, Phase 2b Study to Evaluate the Efficacy and Safety of Ecopipam Tablets in Children and Adolescent Subjects with Tourette's Syndrome

Study Schematic



Did COVID Impact Study Quality?

- Assessment of patient eligibility
 - Data management metrics
 - YGTSS rating quality assessments
- BLINDED**
- External, independent, **unblinded** futility analysis did not reveal any data quality issues
 - **Unblinded** assessment of efficacy ratings including remote evaluations

Central Eligibility Review

Eligibility Review High-Level Results

| Screening Date Range | Total Subjects Reviewed* | Number of Subjects Baselined with No CST Follow-Up | Number of Subjects with Site Follow-up, but Ultimately CST Agreed with Baseline | Number of Screen Failures after and due to CST Consultation |
|----------------------------|--------------------------|--|---|---|
| 27-Nov-2019 to 31-Mar-2020 | 14 | 0 (0%) | 12 (85.7%) | 2 (14.3%) |
| 01-Apr-2020 to 31-Mar-2021 | 122 | 1 (0.8%) | 96 (78.7%) | 19 (15.6%) |
| 01-Apr-2021 to 25-May-2021 | 18 | 0 (0%) | 16 (88.9) | 1 (5.6) |
| Total | 154 | 1 (0.65%) | 124 (80.5%) | 23 (14.9%) |

**Please Note: The number of “Total Subjects Reviewed” also includes the subjects that were reviewed and had no CST follow up, but were screen failed by the PI after they were approved by CST to move forward with enrollment.*

Eligibility Review Details

| Screen Failures after and due to CST Consultation | 27-Nov-2019 to 31-Mar-2020 | | 01-Apr-2020 to 31-Mar-2021 | | 01-Apr-2021 to 25-May-2021 | |
|---|----------------------------|------|----------------------------|-------|----------------------------|------|
| | Totals | % | Totals | % | Totals | % |
| Medical history | 1 | 4.5% | 2 | 9.1% | 0 | 0.0% |
| Lab | 1 | 4.5% | 2 | 9.1% | 0 | 0.0% |
| ECG | 0 | 0.0% | 2 | 9.1% | 0 | 0.0% |
| Other medical | 0 | 0.0% | 0 | 0.0% | 0 | 0.0% |
| Concomitant medications | 0 | 0.0% | 9 | 40.9% | 0 | 0.0% |
| Psychiatric history | 0 | 0.0% | 6 | 27.3% | 1 | 4.5% |
| Primary diagnosis | 0 | 0.0% | 0 | 0.0% | 0 | 0.0% |
| Psychosocial | 0 | 0.0% | 0 | 0.0% | 0 | 0.0% |
| Protocol | 0 | 0.0% | 0 | 0.0% | 0 | 0.0% |
| Other psychiatric | 0 | 0.0% | 0 | 0.0% | 0 | 0.0% |
| Total Screen Failures after and due to CST Consultation* | 2 | | 21 | | 1 | |

What Do DM Metrics Reveal

| Measure | 30 MAR 2020 (N=39) | 30 MAR 2021 (N=93) |
|---|--------------------|--------------------|
| CRF pages opened | 4086 | 15,021 |
| Data entered | 3904 (95%) | 14,991 (94%) |
| CRA Verified | 49% | 84% |
| DM Quality Reviewed | 21% | 55% |
| Edit checks/Queries | 4057 | 15,910 |
| Edit Checks/Queries Resolved | 3732 (92%) | 14,688 (98%) |
| Edit Checks/Queries Unresolved >30 days | 325 (8%) | 333 (2%) |

Introduction

Since the outbreak of COVID-19 there has been a shift in the way that clinical trials are carried out as well as a potential difference in symptom expression across different indications. This may occur for a variety of reasons including isolation, difficulty travelling to a clinic and a range of social, academic and family stressors (e.g., Brooks et al., 2020).

For young people diagnosed with Tourette's syndrome these types of events can often exacerbate symptoms (Hoekstra et al., 2004; Lin et al., 2002; Lin et al., 2007)). The primary scale used to measure tic severity is the Yale Global Tic Severity Scale (YGTSS); the YGTSS is made up of a semi-structured interview, followed by a questionnaire where individuals are asked to rate the severity of their Tic symptoms (both motor and vocal) in domains such as: number, frequency, intensity, complexity, and interference (Leckman et al., 1989).

In this study, a Multicenter, Placebo-Controlled, Double-Blind, Randomized, Parallel-Group, Phase 2b Study to Evaluate the Efficacy and Safety of Ecopipam Tablets in Children and Adolescent Subjects with Tourette's Syndrome, we aimed to examine what, if any, differences there were at screening and baseline visits before and after COVID-19 restrictions were put in place. We chose 11MAR2020 to partition the data (the date the World Health Organization (WHO) declared that COVID was a pandemic) as restrictions on clinical trials begun.

Objectives

The aim of the present study is to assess the potential impact of COVID-19 restrictions on symptom severity at screening and baseline with consideration of motoric and phonic tic severity scores, global tic severity (which is an impairment score that considers psychosocial functioning) and the ability of this and other instruments to capture any such changes. Additionally, are there any individual items of the YGTSS that appeared to change and were the changes captured in other instruments that are used such as the CGI, YBOCS, STAI and others?

Methods

Data were partitioned using the date of 11MAR2020 and screening and baseline YGTSS data were analyzed including total score, phonic and motoric tic severity sub-scores, and the global tic severity score. Additionally, individual item scores were considered across the two time periods. Descriptive statistics were computed using SPSS 27.0 and included means, standard deviation, variance and distribution measures.

Results

YGTSS mean values under consideration did not appear to change significantly between the time periods before and after COVID-19 restrictions began.

Pre-COVID screening mean YGTSS total score at 67.2 with an impairment mean of 32.4 (although impairment scores are only in whole increments of 10 from 0 to 50); thus, impairment represented about 48.2% of the total YGTSS score whereas motoric tics (mean=19.1) and phonic tics (mean=15.6) represented 28.5% and 23.3% respectively. Pre-COVID baseline scores appeared similar to those at screening with a mean impairment of 33.5, a YGTSS total of 68.1 and mean motoric tic score of 19.1 and phonic tic score of 15.4.

Following COVID restrictions the mean YGTSS total score at screening was 66.7 with an impairment mean of 32.8; thus, impairment represented about 49.2% of the total YGTSS score whereas motoric tics (mean=18.6) and phonic tics (mean=15.3) represented 27.8% and 22.8% respectively. Following COVID restrictions the mean baseline impairment score of 32.6 and mean total YGTSS score of 66.9 (motoric mean=18.6 and phonic mean=15.7) do not appear different from pre-COVID baseline scores.

There also were not significant differences in scores on an item level at screening or baseline across the two time periods. Further analysis is pending the receipt of other scale data to determine if there appear to be changes captured by other instruments.

Conclusion

While there does not appear to be a significant change in overall scores on the YGTSS, domain scores or individual item scores, we are awaiting further scale data for measuring other symptom parameters including CGI, YBOCS, STAI and others as well as data around adverse events and drop-out rates.

While it is typical for symptoms of Tourette's to be susceptible to stressors, it was anecdotally noted that many individuals and their families reported less stress in term of the impairment item as opportunities for stressful social interactions in the community or in an educational setting have been greatly reduced.

Our contention is that there may be evidence in other metrics for a difference in the time periods before and after COVID restrictions, but these are not meaningfully reflected in the YGTSS instrument.

References

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Baseline-Week 12 differences

Primary Analyses

Including Remote Assessments

| Scale | PBO | ECO | Δ PBO ECO | P value | PBO | ECO | Δ PBO ECO | P value |
|-----------|--------|--------|------------------|---------|-------|--------|------------------|---------|
| YGTSS-TTS | -6.42 | -9.87 | -3.44 | 0.011 | -3.93 | -7.71 | -3.78 | 0.006 |
| YGTSS-GS | -13.56 | -21.41 | -7.86 | 0.004 | -9.44 | -17.34 | -7.90 | 0.005 |
| CGI-TS-S | -0.53 | -0.91 | -0.37 | 0.027 | -0.39 | -0.76 | -0.37 | 0.028 |
| CGI-TS-I | 3.42 | 3.04 | -0.38 | 0.079 | -3.67 | 3.28 | -0.38 | 0.08 |
| CaGI-TS-I | 3.55 | 2.94 | -0.61 | 0.007 | 4.28 | 3.67 | -0.61 | 0.007 |

Pre & During COVID YGTSS Scores

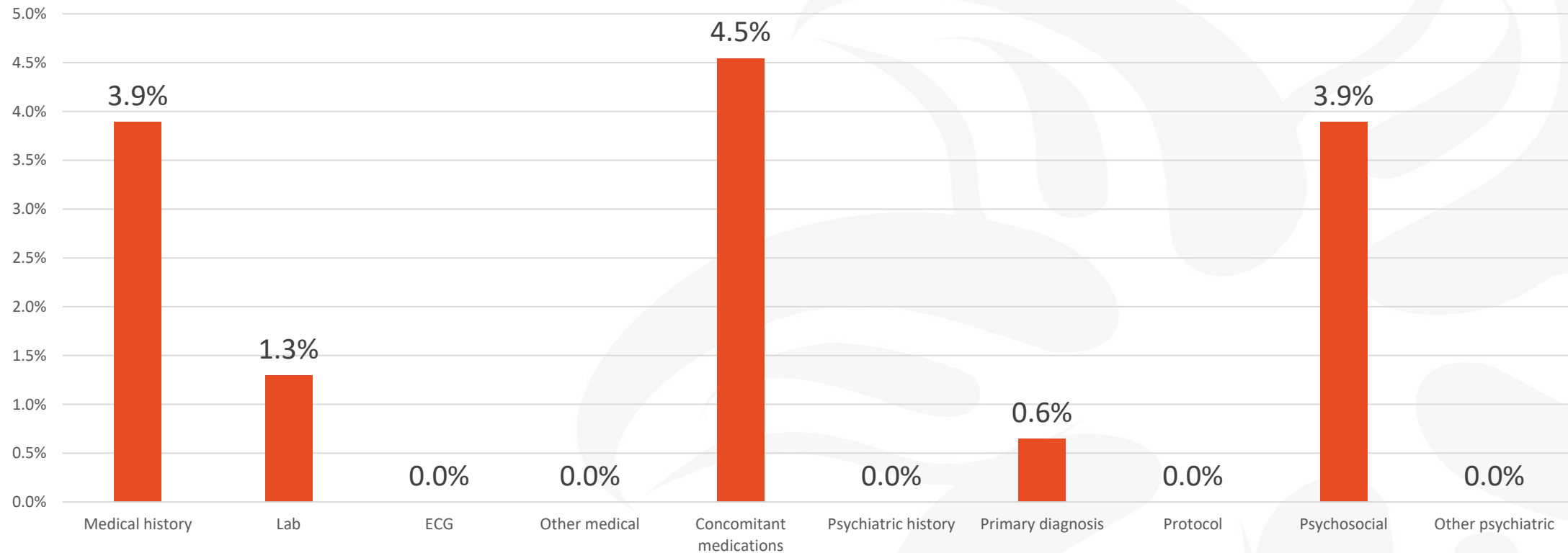
| | Before March 31, 2020 | | | After April 1, 2020 | | |
|-----------|--------------------------------------|---------------------------------|--------------|---------------------------------|-----------------------------|--------------|
| Scale | Mean Baseline to EOT Δ PBO | Baseline to EOT Δ ECO | ABS(PBO-ECO) | Baseline to EOT Δ PBO | Baseline to Δ EOT | ABS(PBO-ECO) |
| YGTSS-TTS | -14.1 | -21.5 | 7.4 | -14.4 | -22.5 | -8.1 |
| YGTSS-GS | -15.3 | -21.2 | 5.9 | -14.9 | -23.7 | 8.8 |

Conclusions

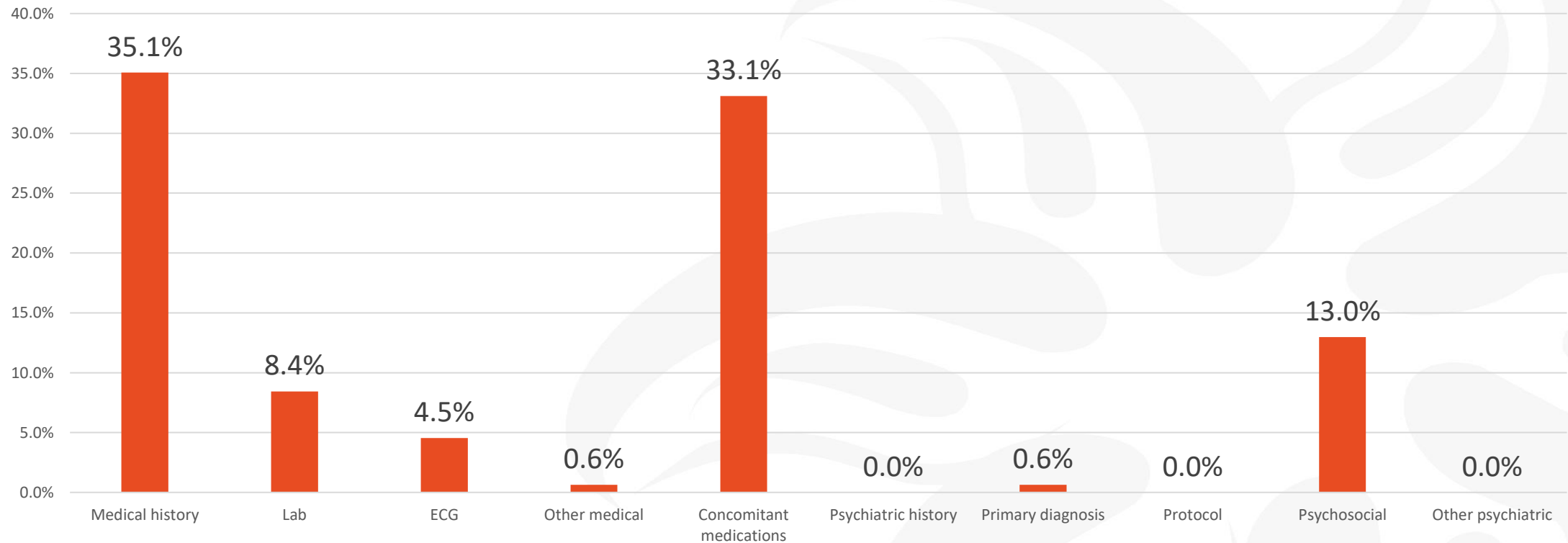
- Quality metrics need to be assessed on an ongoing basis
- Approaches to assess quality vary based on study status
- It is possible to generate high quality data during natural disruptions



CST Follow Up Reasons
27-Nov-2019 to 31-Mar-2020



CST Follow Up Reasons
01-Apr-2020 to 31-Mar-2021



CST Follow Up Reasons
01-Apr-2021 to 25-May-2021

