Conducting a Pediatric Orphan (Tourette's) Study Pre & During COVID Shutdown Experience and Lessons Learned

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Disclosures

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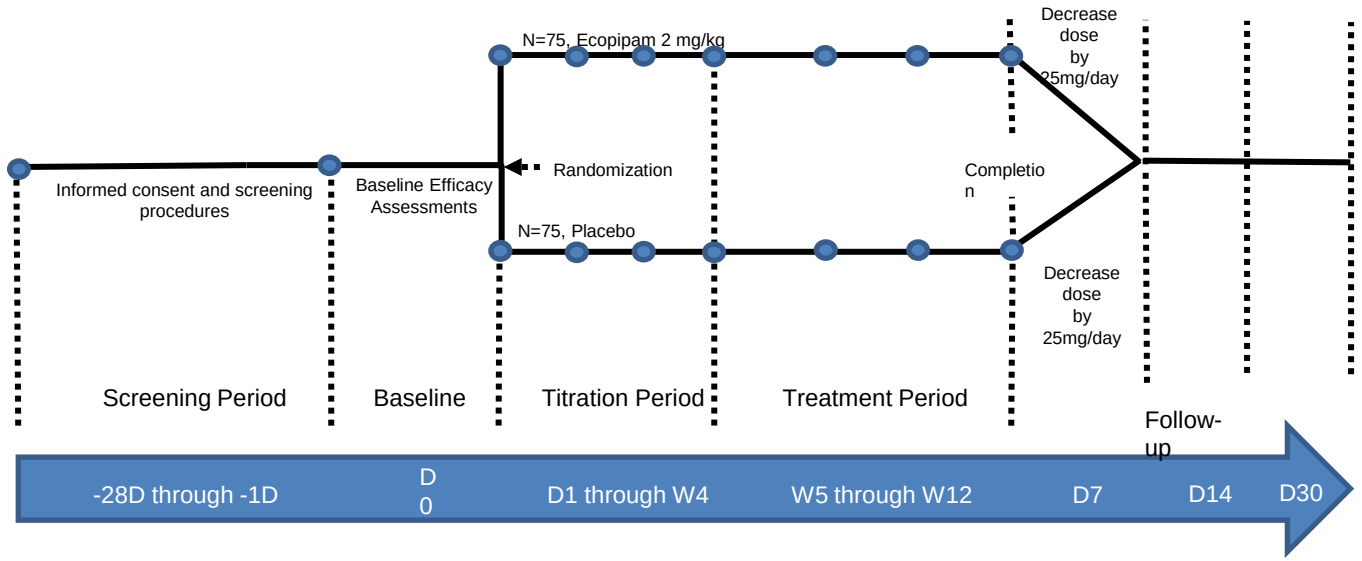
EBS-101-CL-001 Protocol

A Multi-Center, 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



Study Set Up/Conduct

Study Sites

Anticipated approximately 60 sites globally

Countries Proposed

- US
- Canada
- France
- Germany
- Hungary
- Italy
- Poland

Countries Approved

- US
- Canada
- France
- Germany
- Poland

Study Status as of March End 2020

- First site activated in US, MAY 2019
- Number of active sites 39
  - 37 US and 2 Canada
- Number of subjects enrolled: 37

- 11 months 37 subjects enrolled

Impact of COVID-19 on Trials

Questions After Shelter-in-Place

- Should enrolled subjects continue in the study?
- Should new subjects be enrolled in the studies?
- Should site activation continue and new sites be activated to enroll subjects?

Trial Status

- All aspects of study impacted
  - Site activation
  - Subject recruitment
  - Data monitoring
  - Audits
- Mixed response to shelter in place seen
  - Academic sites mostly stopped activities
  - Some non-academic sites stopped; others continued

Principles Guiding Decisions

- Trial participant safety and well being is paramount
- Decisions about subject safety best taken by those directly responsible i.e., PIs/sites
- Sponsor/study team to support decisions taken by PIs/trial participants

- Data quality and trial integrity must be maintained
- Decisions about trial to be taken by sponsor/study team

What Did We do?

- Contacted all sites to ask about continued study participation
  - Sites that opted to not recruit: lower level of contacts
  - Sites that continued to work: more frequent contacts and support

- Maintained awareness of trial ecosystem and regulatory thinking via Webinars arranged by ISCTM and other organizations
- Ensured that IMP could be delivered to subjects
- Protocol amendment to permit remote assessments
- Updated SAP
- Engaged vendors to permit remote assessments and study monitoring visits

March 2021: Trial Status

- Number of active sites 65
  - Canada 3
  - France 2
  - Germany 3
  - Poland 6
  - US 51
- Number of subjects enrolled 130

- 12 months 93 subjects enrolled

Did COVID Impact Study Quality?

- Assessment of patient eligibility
- Assessment of YGTSS ratings/rater quality
- Data management metrics

BLINDED

- External, independent, unblinded futility analysis

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

	27-Nov-2019 to 31-Mar-2020		01-Apr-2020 to 31-Mar-2021		01-Apr-2021 to 25-May-2021	
Screen Failures after and due to CST Consultation	**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%
Reviewed for quality by DM	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%)

Futility & Safety Analysis

- Futility & safety analysis conducted after 75 subjects completed study
  - 37 randomized before shelter-in-place instituted
  - 38 randomized after shelter-in-place instituted
- Conducted by external, independent, unblinded expert panel

- Recommendation
  - No data quality issues identified
  - Continue study as planned

LESSONS

- Be flexible
- Listen to sites
- Changes may need to be individualized
- Communicate Communicate Communicate
- Use all means of communication that are available

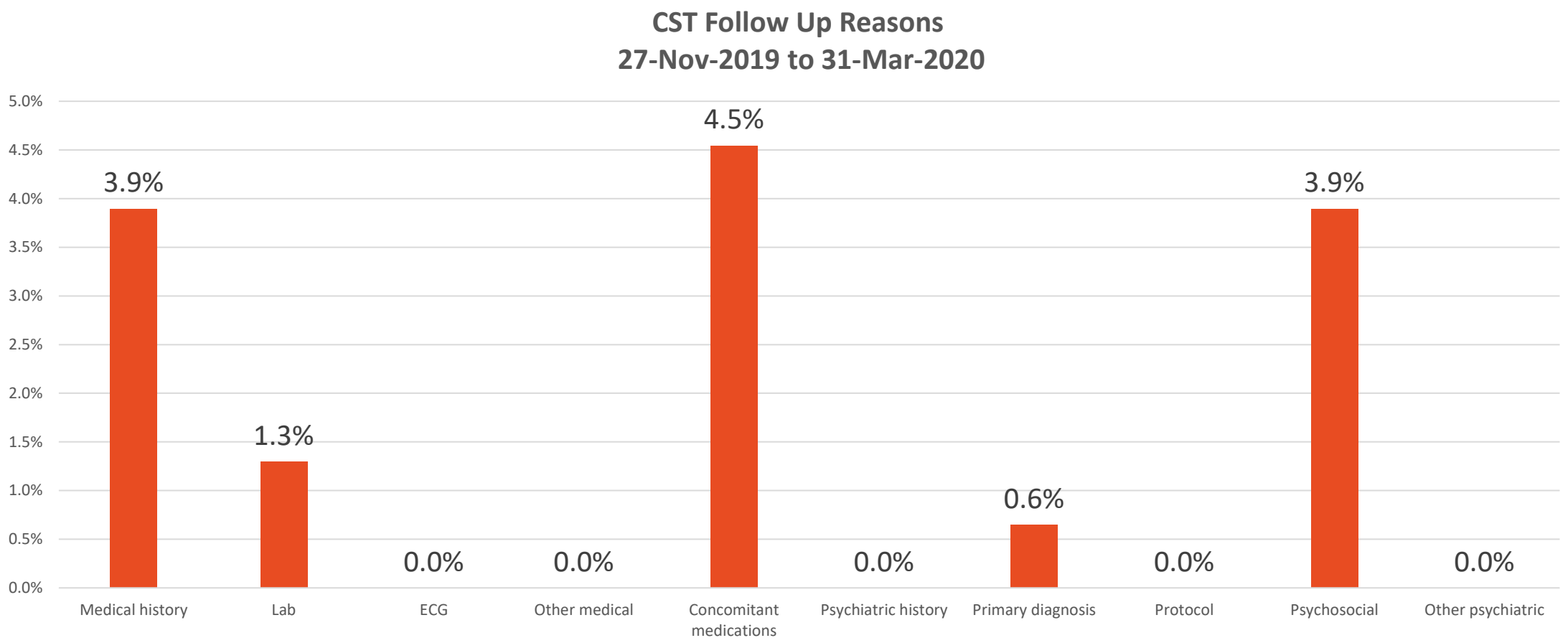
OVERARCHING LESSONS

- Know and follow your principles

- Lesson is learned only if you act on what you have learned

BACKUP

Eligibility Review Follow up Reasons



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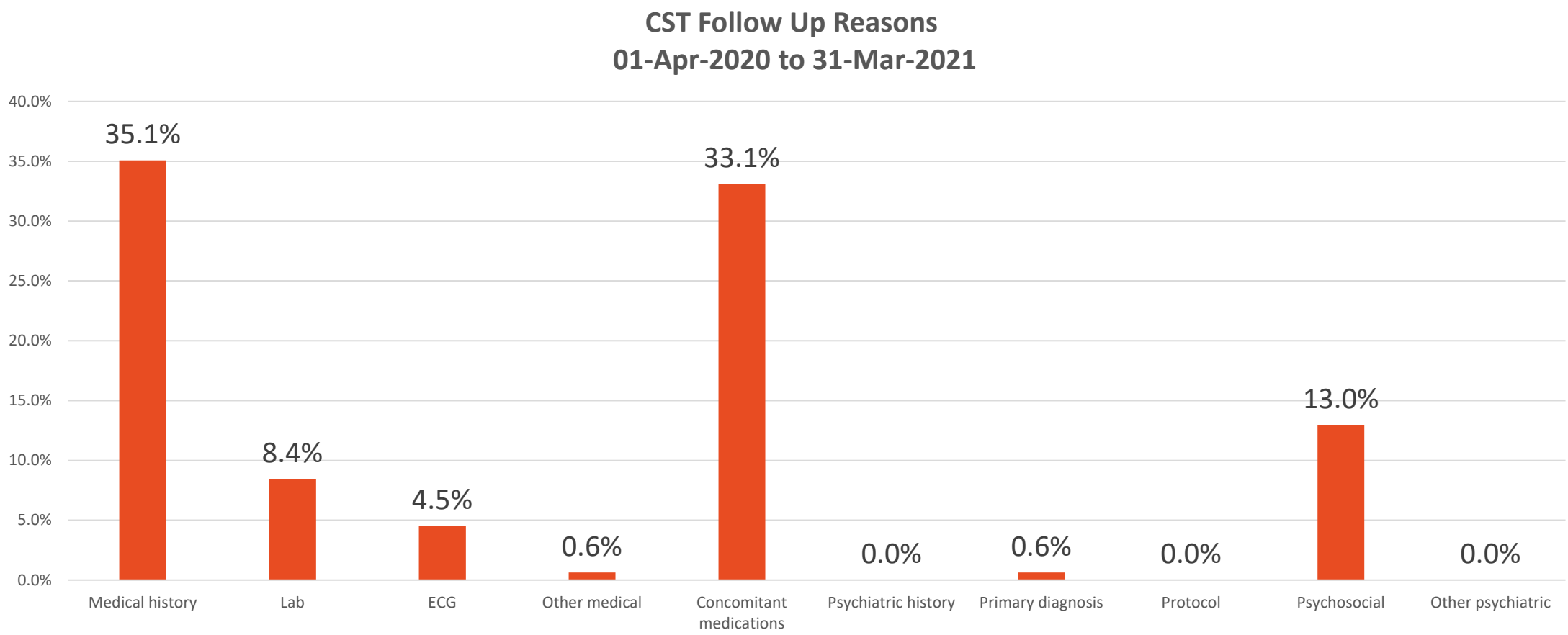

Eligibility Review Follow up Reasons