P005 LONG-TERM SAFETY AND EFFICACY OF SOLRIAMFETOL FOR EXCESSIVE DAYTIME SLEEPINESS: AN OPEN-LABEL EXTENSION RANDOMISED WITHDRAWAL TRIAL

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Introduction Solriamfetol (formerly JZP-110), a dopamine and norepinephrine reuptake inhibitor, has been approved in the United States to improve wakefulness in adults with excessive daytime sleepiness (EDS) associated with narcolepsy (75–150 mg) or obstructive sleep apnoea (OSA; 37.5–150 mg). A Marketing Authorisation Application for these indications is under review with the European Medicines Agency. This study evaluated the long-term safety and efficacy of solriamfetol.

Methods Participants with EDS associated with narcolepsy or OSA who completed prior solriamfetol studies initiated open-label treatment with a 2-week titration phase followed by a maintenance phase of ≤50 weeks. A 2-week, placebo-controlled, randomised withdrawal (RW) phase was conducted after 6 months. Change from beginning to end of the RW phase in Epworth Sleepiness Scale (ESS) was the primary endpoint; Patient and Clinician Global Impression of Change (PGI-C and CGI-C, respectively) were secondary endpoints.

Results Safety population comprised 643 participants (226 narcolepsy; 417 OSA); 280 participants (141 placebo; 139 solriamfetol) comprised the RW modified intent-to-treat population. A total of 458 participants (71%) completed the study. Maintenance of efficacy in this 1-year study was demonstrated on the ESS, PGI-C, and CGI-C. Least squares mean change from the beginning to the end of the RW phase in ESS score was 5.3 versus 1.6 in participants randomised to placebo or solriamfetol, respectively (P<0.0001). Greater percentages of participants randomised to placebo versus solriamfetol in the RW phase reported as worse on PGI-C and CGI-C (both P<0.0001). The most frequent adverse events (AEs; ≥5%) were headache, nausea, nasopharyngitis, insomnia, dry mouth, anxiety, decreased appetite, and upper respiratory tract infection; 27 (4.2%) participants had ≥1 serious AE.

Discussion These results demonstrate the long-term efficacy of solriamfetol for EDS in participants with narcolepsy or OSA. Safety profile following long-term administration was consistent with prior solriamfetol studies.

Support Jazz Pharmaceuticals.

P006 MODELLING SLEEP-WAKE TRANSITIONS IN VERY AND MODERATELY PRE-TERM INFANTS

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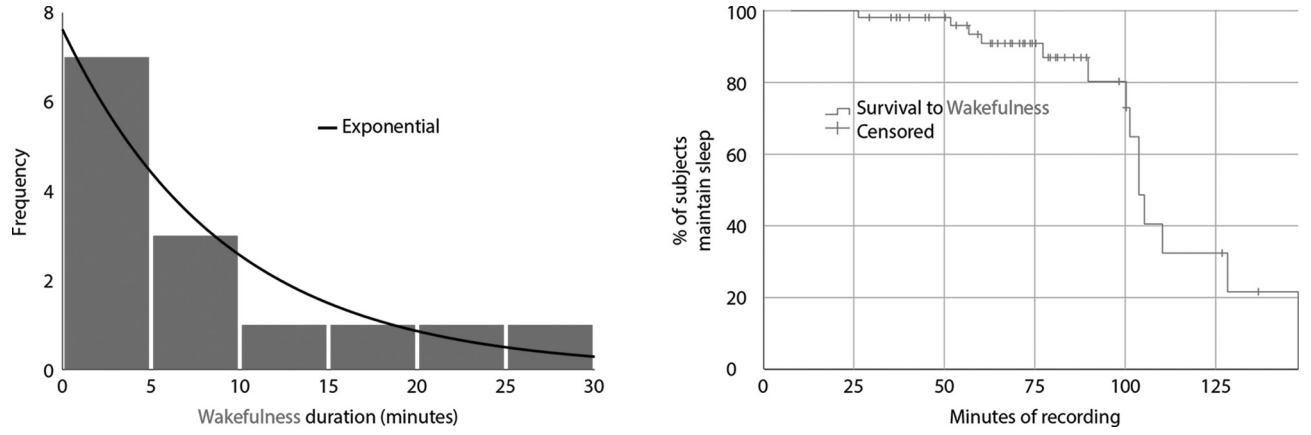
Introduction Sleep is the dominant vigilance state in pre-term infants, but its regulation is still poorly understood, with no underpinning quantitative framework.

In animal studies, neonatal sleep-wake characteristics follow statistical patterns, e.g. wakefulness durations exhibit an exponential distribution.[1] Here we investigated whether the same holds true for pre-term human infants.

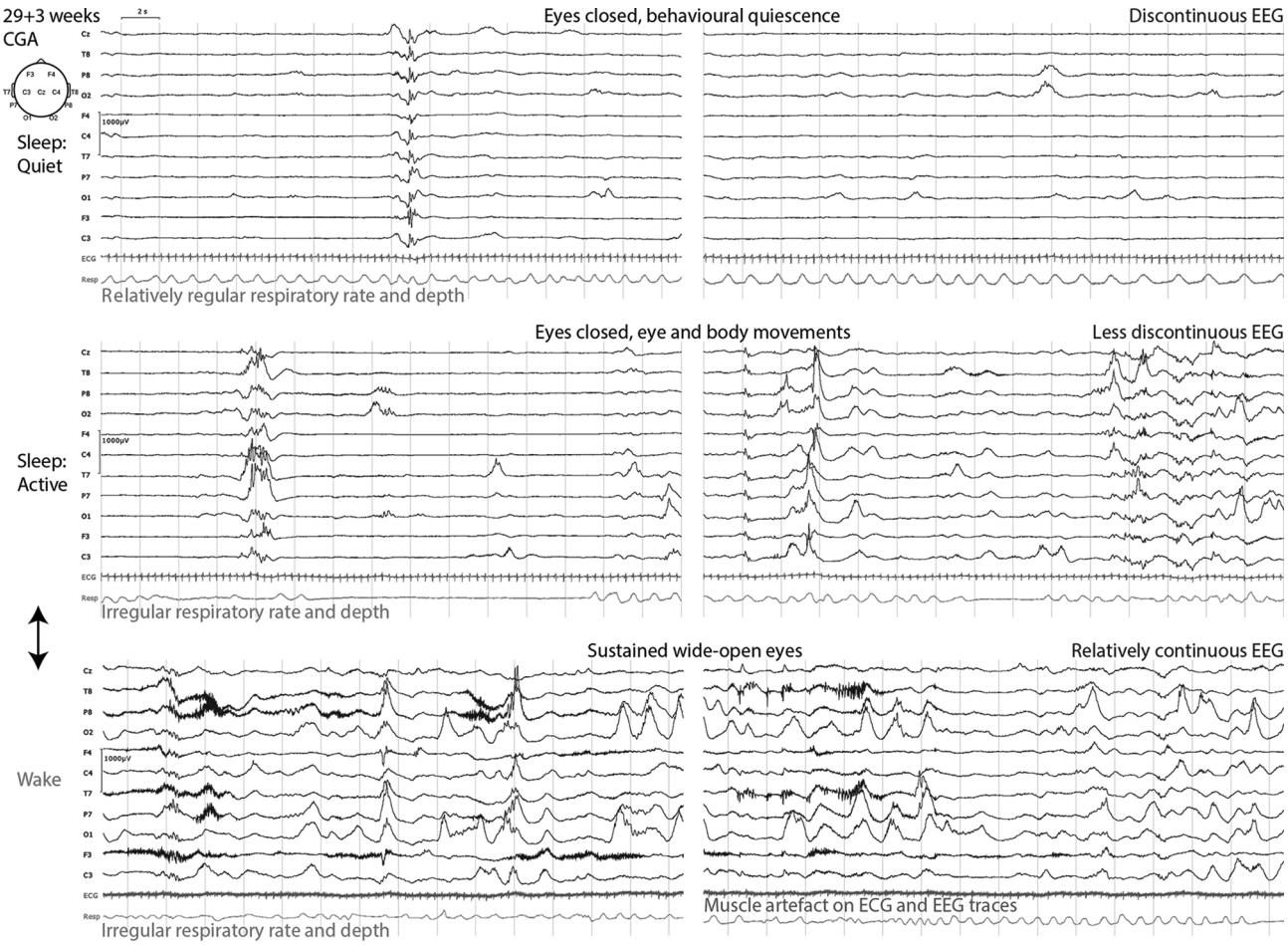
Methods We recorded electroencephalography (EEG), respiratory movement, electrocardiography (ECG), and behavioural observations for up to two hours from 54 non-mechanically ventilated infants being cared for on the neonatal unit (28+2–34+1 weeks+days corrected gestational age). Data were staged as sleep or wakefulness in 30-s epochs (figure 1).

We characterised i) the distribution of wakefulness durations, using the Kolmogorov-Smirnov goodness-of-fit test, and ii) the likelihood of transitioning from sleep to wakefulness during the recording, using the Kaplan-Meier estimator which takes account of censored observations, i.e. when the event of interest (wakefulness) was not captured.

Results 14/54 (26%) infants cycled through wakefulness during the recording: durations ranged from 2 to 29 minutes and



Abstract P006 Figure 1



Abstract P006 Figure 2

did not deviate significantly from an exponential distribution ($D(14)=0.733$, $p=0.657$) (figure 2 left).

There is a sharp increase in the likelihood of transitioning from sleep to wakefulness when recordings increase from 93 to 96 minutes, when the estimated percentage of subjects maintaining sleep falls from 75 to 50%. Nevertheless, 25% of subjects will still be asleep at 121 minutes (figure 2 right).

Discussion In pre-term infants, the durations of awakenings are exponentially distributed, as in neonatal animals.[1] The likelihood of awakening does not increase linearly with recording duration, but is gated after approximately 100 minutes, demonstrating cyclicity. Future work will build on these preliminary data to model how demographic and environmental variables (e.g. necessary painful procedures) influence the neonatal sleep-wake cycle.

REFERENCE

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P007 10 YEAR SLEEP SERVICE DELIVERY TRENDS IN A LARGE DISTRICT HOSPITAL

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Introduction Optimal continuous positive airway pressure (CPAP) use is essential in the successful treatment of obstructive sleep apnoea (OSA), but optimising CPAP therapy is a challenge.

Methods We set out to outline our CPAP service trends in the last 10 years. We quantified the proportion of patients diagnosed with moderate or severe OSA from studies completed from samples from 2009. We recorded CPAP compliance at first review, and the time it took for patients to reach adequate treatment compliance.

Results We found an increasing trend in studies completed over the last decade, although the proportion of patients diagnosed with moderate or severe OSA did not reflect an increase, with only 20% of patients receiving a diagnosis of moderate or severe OSA recently. The majority of patients (61%) were compliant with CPAP therapy at their first review. Although it took on average 4 to 5 months for patients to reach adequate CPAP compliance, this trend decreased over 10 years. Almost half of patients prescribed CPAP 10 years ago remain under regular biennial reviews, and an average of 20% of patients were intolerant to CPAP.

Discussion Referrals to our service increased over the last decade. Although screening criteria for referrals became more specific for obstructive sleep apnoea, the proportion of moderate and severe diagnoses has shown a downward trend. There is an increasing demand on our service, with more referrals and more complex referrals unrelated to OSA. CPAP compliance remains a challenge, without improvements in compliance trends despite improvements in technology and equipment. Finally, our results highlight that although the majority of