CONCERTA® (methylphenidate HCl ER)
CONCERTA - Use of a Drug Holiday

SUMMARY

- The decision to take a drug holiday due to concerns over side effects or long-term effects should be carefully considered. Stimulants are only effective as long as they are given, and discontinuation may result in a rapid return of symptoms.[1]
- Data from a long-term study of CONCERTA showed that height, weight, and Body Mass Index (BMI) Z scores and malnutrition index were not significantly different in patients who took drug holidays of ≥30 days as compared with those who did not.[2]
- In a study of 40 boys with ADHD, use of weekend holidays for methylphenidate (MPH) treatment showed a reduction in side effects such as insomnia and decreased appetite with no significant decrease in efficacy in the short-term.[3]
- Subanalysis of a long-term study of CONCERTA showed that practitioners may be able to predict who is more likely to take a drug holiday and thus prevent lower outcomes associated with nonadherence.[4]

BACKGROUND

According to the American Academy of Child & Adolescent Psychiatry, the decision of parents to stop their children's stimulant medication, known as a "drug holiday", because of concerns over side effects such as lack of weight gain or long-term drug effects of the medication, should be carefully weighed.[1] Stimulant medications only work as long as they are taken, so treatment discontinuation trials should only take place at times other than when the child has important school or social activities.

CLINICAL DATA

Spencer et al (2006)[2] analyzed growth data from children with ADHD taking CONCERTA for at least 21 months (N=407).

Study Design/Methods

- Open label, 24-month study
- Children, aged 6 to 13 years, who completed at least 21 months of the open-label study were included in this analysis.
- Subjects were assigned to one of three doses of CONCERTA (18 mg, 36 mg or 54 mg).
- Doses could be adjusted up or down based on the physician rater's assessment; doses could be reduced or medication could be stopped on weekends or for drug holidays during vacation periods.
- During the study, subjects attended clinic visits at monthly intervals during the first year, then every three months, where height, weight, blood pressure, and heart rate were recorded.
- Height and weight data were used to calculate BMI, age-corrected height (height Z score), age-corrected weight (weight Z score), age-corrected BMI (BMI Z score), height deficit, weight deficit, BMI deficit, and malnutrition index.

Results

- Of the 407 children who entered the open-label study, 178 received treatment for at least 21 months and had height and weight measurements at baseline and the 21-month time point.
- The mean daily dose of CONCERTA increased from 34.3 mg at the beginning of the study to 43.7 mg through the course of the study.
- The weight-adjusted dose increased from 1.1 mg/kg/day at baseline to 1.2 mg/kg/day at month 21.

- Data were analyzed comparing subjects who took ≥30 total days of drug holidays throughout the 21-month period (n=50) versus those who reported <30 total days without medication throughout the study (n=120).
- Differences between these two groups in changes in Z scores and malnutrition index during the course of the study were not statistically significant as displayed in Table: Changes in Z Scores and Malnutrition Index.

Changes in Z Scores and Malnutrition Index

Change in:	≥30 days	<30 days	P value
Weight Z Score	-0.175	-0.274	0.183
Height Z Score	+0.012	-0.083	0.156
BMI Z Score	-0.259	-0.303	0.599
Malnutrition Index	-0.034	-0.039	0.736

Martins et al (2004)[3] conducted a study in male children with ADHD to assess whether the efficacy and tolerability of MPH would be affected by weekend drug holidays (N=40).

Study Design/Methods

- 28-day double-blind study
- Patients, ages 6 to 14 years, were randomized to either twice-daily MPH for 7 days a week or twice daily MPH on weekdays and placebo on weekends.
- Doses for the first week began at 0.3 mg/kg/day and increased to 0.5 mg/kg/day on the second week and to 0.7 mg/kg/day on the third and fourth weeks (as tolerated).
- The primary efficacy assessment was the change from baseline on the Conners' Abbreviated Rating Scale (ABRS) as assessed by parents and teachers.
- Parents completed the Barkley's Side Effect Rating Scale (SERS) to assess side effects on weekends.

Results

- There was a significant reduction in ABRS scores between pretreatment and endpoint treatment in both teacher and parent ratings for both groups.
- No significant difference was detected on endpoint ABRS ratings between the groups.
- Analysis of side effects showed a significant effect of drug holiday on reducing insomnia and a trend towards a reduction in decreased appetite as compared to the continuous treatment group without a significant reduction in parental ratings of efficacy.

Faraone (2003)[4] assessed adherence to treatment and predictors of nonadherence in children with ADHD receiving CONCERTA (N=407).

Study Design/Methods

- Subanalysis of a long-term, open-label study
- Children (aged 6-13 years) received CONCERTA at doses of 18, 36, or 54 mg, titrated to optimal response and tolerance.
- Drug holidays were allowed on weekends and during vacation periods.

Results

- After one year, data were available for 289 subjects.
- Drug holidays were taken by 32% of the subjects.
- Several baseline factors were found to be predictors of subjects who would take drug holidays: older age of the subject, inattentive ADHD subtype, fewer baseline ADHD symptoms, lower starting dose of CONCERTA, and minority ethnic status.
- On follow-up, nonadherence was associated with significantly poorer treatment efficacy at home but not at school.

LITERATURE SEARCH

A literature search of MEDLINE®, Embase®, BIOSIS Previews®, and Derwent Drug File (and/or other resources, including internal/external databases) was conducted on 05 March 2024.

REFERENCES

1. Practice parameter for the use of stimulant medications in the treatment of children, adolescents, and adults. *J Am Acad Child Adolesc Psychiatry*. 2002;41(suppl 2):26S-49S.
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3. Martins S, Tramontina S, Polanczyk G, et al. Weekend holidays during methylphenidate use in ADHD children: a randomized clinical trial. *J Child Adolesc Psychopharmacol*. 2004;14(2):195-205.
4. Faraone S. Impact of drug holidays on ADHD children treated with OROS methylphenidate. Poster presented at: The 50th Anniversary Meeting of the American Academy of Child and Adolescent Psychiatry; October 14-19, 2003; Miami, FL.