

Results of the Analysis of Suicidality in Pediatric Trials of Newer Antidepressants

Psychopharmacologic Drugs Advisory Committee and the Pediatric Advisory Committee
September 13-14, 2004

Tarek A. Hammad, MD, PhD, MSc, MS

Senior Medical Reviewer



Division of Neuropharmacological Drug Products
Center for Drug Evaluation and Research, FDA



Data Domain

- 25 trials conducted in pediatric patients in nine drug development programs + TADS trial
- Drugs - number of trials:
 - SSRIs
 - Citalopram (Celexa) - 2
 - Fluoxetine (Prozac) - 4 + TADS
 - Fluvoxamine (Luvox) - 1
 - Paroxetine (Paxil) - 6
 - Sertraline (Zoloft) - 3
 - Atypical antidepressants
 - Bupropion (Wellbutrin) - 2
 - Mirtazapine (Remeron) - 1
 - Nefazodone (Serzone) - 2
 - Venlafaxine (Effexor XR) - 4



2

Data Domain, continued ...

- Indications - number of trials
 - Major Depressive Disorder (MDD) - 15 (+ TADS)
 - Anxiety Disorders
 - Obsessive Compulsive Disorder - 5
 - Generalized Anxiety Disorder - 2
 - Social anxiety Disorder/Social Phobia - 1
 - Attention Deficit Hyperactivity Disorder - 2
- Two trials excluded (Paxil 453-relapse prevention, Wellbutrin 41-uncontrolled)
- Trial year: 1983 to 2004
- Duration: 4 to 16 weeks



3

Overall relative risks (RR) of suicidal behavior or ideation (codes 1, 2, & 6) by drug

Drug	Relative Risk (95% CI), MDD trials	Relative Risk (95% CI), all trials, all indications
Celexa	1.37 (0.53, 3.50)	1.37 (0.53, 3.50)
Luvox	No MDD trials	5.52 (0.27, 112.55)
Paxil	2.15 (0.71, 6.52)	2.65 (1.00, 7.02)
Prozac *	1.53 (0.74, 3.16)	1.52 (0.75, 3.09)
Zoloft	2.16 (0.48, 9.62)	1.48 (0.42, 5.24)
Effexor XR	8.84 (1.12, 69.51)	4.97 (1.09, 22.72)
Remeron	1.58 (0.06, 38.37)	1.58 (0.06, 38.37)
Serzone	No events	No events
Wellbutrin	No MDD trials	No events



* Note that TADS data are added to Prozac

4

Robustness of the risk estimates of suicidal behavior or ideation (codes 1,2, & 6) to event ascertainment: results of outcome 4 "possible suicidal behavior or ideation"

Outcomes	Overall RR (95% CI), all trials, all indications	Overall RR (95% CI), SSRI MDD trials
Suicidal behavior or ideation (codes 1,2, & 6)	1.95 (1.28, 2.98)	1.66 (1.02, 2.68)
Possible suicidal behavior or ideation (codes 1, 2, 6 + 3, 10)	2.19 (1.50, 3.19)	1.91 (1.27, 2.89)

- The signal was slightly altered
- Note that TADS data are added to all analyses



5