Update on Pfizer’s New Pharmacotherapy - Varenicline

New York State Department of Health Cessation Center Collaborative Statewide Conference Call
September 7, 2005

David Gonzales, PhD
Co-Director
OHSU Smoking Cessation Center
Division of Pulmonary & Critical Care Medicine
Oregon Health & Science University
gonzales@ohsu.edu
Varenicline and how it might work

- New compound developed by Pfizer Inc. specifically for the indication of smoking cessation.\(^1\)
- Novel selective \(\alpha_4\beta_2\) nicotinic receptor partial agonist.\(^1\)
- Activation of the receptor by varenicline would be expected to reduce symptoms created by the withdrawal of nicotine from the receptor.\(^1\)
- Supplied in tablet form for oral administration.
- Not yet submitted to the FDA for approval.

\(^1\)Oncken C, et al. (2005). Presented at the 2005 Meeting of the Society for Research on Nicotine and Tobacco. Prague, Czech Republic
7-Week trial of varenicline, bupropion and placebo

- Multicenter, randomized double blind trial
- 3 doses of varenicline plus bupropion plus placebo.
  - 0.3 mg varenicline once daily for 6 weeks
  - 1.0 mg varenicline once daily for 6 weeks
  - 1.0 mg varenicline twice daily for 6 weeks
  - 150 mg bupropion once daily for 3 days followed by 150 mg twice daily for the balance of 7 weeks.
  - Placebo for 7 weeks.

Results of 7-week phase 2 trial of varenicline, bupropion and placebo (n = 503)

- Study design compared each drug to placebo rather than to each other. Further study will be needed to directly compare varenicline vs. bupropion.

- Results are for continuous abstinence for any 4 week period.
  - 0.3 mg varenicline once daily = 28.6%
  - 1.0 mg varenicline once daily = 37.3%
  - 1.0 mg varenicline twice daily = 48.0%
  - 150.0 mg bupropion twice daily = 33.3%
  - Placebo = 17.1%

7-week trial: safety and tolerability of varenicline

- Nausea was the most common adverse experience (AE) related to varenicline and was mainly mild to moderate in severity.

- Percent discontinued due to any treatment emergent AE.
  - 0.3 mg varenicline once daily = 14.3%
  - 1.0 mg varenicline once daily = 12.7%
  - 1.0 mg varenicline twice daily = 11.2%
  - 150.0 mg bupropion twice daily = 15.9%
  - Placebo = 9.8%

Results of 12-week phase 2 varenicline dosing trial (n = 627)

- 4 doses evaluated:
  - .5 mg and 1.0 mg twice daily titrated
  - .5 mg and 1.0 mg twice daily non-titrated.

- Weeks 9-12 continuous abstinence rates pooled by dose.
  - 1.0 mg twice daily doses = 50.6%
  - 0.5 mg twice daily doses = 45.1%
  - Placebo = 12.4%

12-week trial: safety and tolerability of varenicline & effects on withdrawal symptoms

- Generally well tolerated.
- No safety issues of concern in results of clinical lab tests, ECG’s and vital signs.
- Discontinuation due to treatment emergent AE’s similar to placebo.
- Nausea remains a common AE, but incidence was reduced in those taking twice daily titrated doses.
- Withdrawal symptoms reduced: craving, smoking satisfaction and psychological reward.

Summary

- Results of Phase 2 clinical trials for varenicline, a novel partial nicotine agonist, for smoking cessation are promising.
- Results from additional studies are currently being analyzed and will be presented in the Fall of 2005.
- Some late Phase 3 trials are still underway.
- Submission to the FDA is likely in 2006.
New Pharmacotherapies create opportunities for providers and patients

- Pfizer and Sanofi-Aventis each are conducting trials of new smoking cessation drugs that could complete the FDA review process in 2006 or 2007.
- Advertising related to the launch of new smoking cessation drugs will increase consumer demand for smoking cessation in general.
- Providers will have increased opportunities to talk to patients about all smoking cessation options, including the new one(s).
- Pharmaceutical companies with new cessation drugs, as well as those with existing ones, may support provider training in smoking cessation such as CME presentations or unrestricted educational grants.