P-302  
**BLOOD PRESSURE AND CARDIOVASCULAR EFFECTS OF TADALAFIL, A NEW PDE5 INHIBITOR**  
A. M. Hutter, Jr., R. A. Kloner, V. Watkins, T. Costigan, A. Bedding, M. Mitchell, J. Emmick. Massachusetts General Hospital, Harvard Medical School, Boston, MA, United States; University of Southern California, Los Angeles, CA, United States; Eli Lilly and Company, Indianapolis, IN, United States.

In the Massachusetts Male Aging Study, the age-adjusted probability for complete impotence in men with treated hypertension was 1.4%, vs 9.6% in the entire sample of 1,290 men aged 40 to 70 (Feldman et al. N Engl J Med. 1994;151:54-61).

Tadalafil, a selective and potent inhibitor of PDE5, is a new treatment for men with erectile dysfunction (ED). Tadalafil and other PDE5 inhibitors potentiate vascular smooth muscle relaxation; therefore, they may affect the cardiovascular (CV) system as well. PDE5 inhibitors have been shown to augment the hypotensive effects of nitrates; PDE5 inhibitors and nitrates both act through the nitric oxide-cGMP pathway. This report summarizes the CV profile of tadalafil based on clinical pharmacology and large-scale clinical trials.

In healthy subjects receiving 20 mg of tadalafil, there was no significant difference in standing systolic and diastolic blood pressure compared to subjects receiving placebo (mean maximal decrease of 0.2 and 4.6 mm Hg, respectively). There was also no change in heart rate.

Sadovsky et al determined an incidence rate of myocardial infarction (MI) of 0.6 per 100 patient-years in age-standardized men (Sadovsky et al. Int J Clin Pract. 2001;55:115-128). Across all clinical studies of tadalafil, the rate of MI in treated patients (N=4000) was 0.39, vs 1.1 in patients receiving placebo (N=1200).

The phase 3 clinical trials included patients with a wide variety of stable CV conditions, including patients taking multiple antihypertensive agents. Overall, the incidence of CV adverse events (AEs) in these trials was low, and the rate of AEs reported by patients on tadalafil was similar to placebo. There were no reports of hypotension for tadalafil-treated patients and 1 report for a placebo-treated patient. (The table shows treatment-emergent CV AEs occurring in at least 0.5% of patients receiving placebo or tadalafil. The number of syncope reports was too small for calculation of significance.)

In conclusion, tadalafil treatment has not been associated with an increased incidence of CV events. In addition, tadalafil has little effect on systemic arterial pressure.

<table>
<thead>
<tr>
<th>Event</th>
<th>Placebo (N = 379)</th>
<th>Tadalafil (N = 949)</th>
<th>P Value (AB NS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flushing</td>
<td>1.6%</td>
<td>3.7%</td>
<td>0.089</td>
</tr>
<tr>
<td>Dizziness</td>
<td>1.9%</td>
<td>2.4%</td>
<td>0.873</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.6%</td>
<td>1.1%</td>
<td>0.912</td>
</tr>
<tr>
<td>Syncope</td>
<td>0.5%</td>
<td>0.1%</td>
<td>NA</td>
</tr>
</tbody>
</table>

Key Words: PDE5 Inhibition, Tadalafil, Erectile Dysfunction

P-303  
**THE RELATIONSHIP BETWEEN DIETARY FIBER INTAKE AND THE PREVALENCE OF HYPERTENSION**  
Priscilla Samuel, Debra R. Keast. John Stuart Research Laboratories, The Quaker Oats Company, Barrington, IL, United States; Food Science and Nutrition, Michigan State University, East Lansing, MI, United States.

One in five Americans has high blood pressure, yet a third are not aware of their condition. To date, an impressive body of evidence supports the beneficial effect of diet on this highly prevalent and deadly, yet modifiable risk factor. Soluble viscous fiber has been recognized for its role in reducing blood cholesterol and emerging clinical data on dietary fiber from whole grain oats provides some evidence for its role in also reducing blood pressure. The objective of this study was to examine the relationship between dietary fiber and hypertension, using a nationally representative sample of adults 40 y and older from the NHANES III, 1988-1994. We evaluated the prevalence of hypertension and patterns in mean systolic and diastolic blood pressure by tertiles of total, soluble, and insoluble dietary fiber intakes. Consistent with the clinical definition of high blood pressure in the JNC VI, high blood pressure was defined as mean systolic blood pressure ≥140 mm Hg, mean diastolic blood pressure ≥90 mm Hg, or current use of antihypertensive medication. For tertiles of total dietary fiber intake, 47% vs. 44% of all adults 40+ y had hypertension in the lowest vs. highest tertiles. Additionally, adults 55+ y were twice as likely to have hypertension than those 40-54 y, across almost all tertiles of fiber intake, for both men and women. The findings were consistently significant for women 40-54 y, in that, 30 vs. 21% in 24% in the lowest, middle and highest tertiles of total fiber intake had hypertension, with similar findings for tertiles of insoluble and with men for soluble fiber intakes. As previously observed, we found that mean systolic and diastolic blood pressure increased with age. By tertiles of total fiber intake, mean diastolic blood pressure was significantly higher in the lowest versus middle tertiles for men 40-54 y. For adults 40+y, and the subgroup 40-54 y, mean systolic blood pressure was significantly higher in the lowest vs. highest tertiles of insoluble fiber intake (Adults 40+ y: 133 ±0.7 vs. 131 ±0.6 mm Hg), and for soluble fiber, similar patterns were observed but did not reach significance. These findings support new and emerging clinical data, suggesting that increased dietary fiber intakes may also help reduce blood pressure therefore, the implications are relevant for education, prevention and management of hypertension. Furthermore, implementation of dietary modifications with a proven ability to lower blood pressure can have a notable impact on the prevalence of hypertension in the US.

Key Words: Dietary Fiber, Prevalence, Blood Pressure

P-304  
**ASSOCIATION OF CYP1A1, ACE AND P22PHOX POLYMORPHISMS WITH ESSENTIAL HYPERTENSION IN POSTMENOPAUSAL WOMEN**  
Vasco Lanca,1 Constanca Coelho,1 Peter Pego,2 Helena Moreira,2 Luis Sardinha,2 Paula Alcantara,3 Joao Bicho.1 Genetics Laboratory, Lisbon School of Medicine, Lisbon, Portugal; 2School of Human Motricity, Lisbon, Portugal; 3Internal Medicine Department, Hospital Santa Maria, Lisbon, Portugal.

The aim of this study was to determine the role of CYP1A1 T6325C, p22phox C242T and ACE I/D genotypes in HD in postmenopausal (PM) women.

The studied population consisted of 96 normotensive postmenopausal women and 26 postmenopausal women with hypertension (I: CYP1A1 T6325C, p22phox C242T and ACE I/D were determined by PCR-RFLP and PCR.

Cytochrome P4501A1 (CYP1A1) catalyses the hydroxylation of omeprazol and arachidonic acid (AA), producing vasoactive substances, rendering the CYP1A1 a candidate predisposition gene for HD. The D allele of the angiotensin converting enzyme (ACE) I/D polymorphism is a genetic risk factor for HD and is responsible for a higher ACE activity. Angiotensin II (Ang II) generated by ACE activates, among other actions, the first step of AA production. Ang II also activates a membrane NAD(P)H oxidase of which p22phox is an essential subunit, producing superoxide anions. The p22phox C242T gene polymorphism has been associated, in some populations, with several cardiovascular conditions, but this association remains controversial. PM women with the C allele of the CYP1A1 T6325C polymorphism, associated with a higher cytochrome P4501A1 activity, have an increased risk of HD (OR = 2.9, 95%, CI: 1.1-7.5). Women with both the C allele of the CYP1A1 T6325C and the D allele of the ACE I/D polymorphisms present an increased risk of HD (OR = 3.9, 95%, CI: 1.2-12.0). No differences were found regarding the p22phox C242T polymorphism.