EPH140

Safety of PDE5 Inhibitors for Erectile Dysfunction: Descriptive and Disproportionality Analyses of FAERS from 2010 to 2022

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INTRODUCTION

- Phosphodiesterase type 5 inhibitors (PDE5Is): first-line therapy for erectile dysfunction (ED)
  - **Common side effects**: headache, indigestion, nasal stuffiness, mild visual changes, myalgia, and hypotension and dizziness
  - **Clinically important side effects**: non-arteritic anterior ischemic optic neuropathy, hearing loss, priapism, melanoma, and prostate cancer
- Limited research in post-marketing surveillance databases analyzing safety of PDE5Is for ED

OBJECTIVES

Identify **characteristics of adverse events (AEs)** and any **potential safety signals** associated with PDE5Is used for ED from a post-marketing safety surveillance program

METHODS

- Retrospective study for all reported AEs associated with PDE5Is in FDA Adverse Event Reporting System (FAERS) database between January 2010 and June 2022
- Excluded any indication other than ED
- AEs grouped by disease categories and by FAERS-defined outcomes
- Disproportionality analysis: reporting odds ratio (ROR) & proportional reporting ratio (PRR)
- Signal must be simultaneously detected by PRR and ROR
  - PRR: number of events ≥ 3 & **PRR ≥ 2**
  - ROR: lower limit of **95% confidence interval > 1**
  - Chi-squared with Yates correction ≥ 4 → p-value < 0.05*

KEY FINDINGS

- Total of **29,176 total AEs** reported for 4 PDE5Is between January 2010 and June 2022
  - **Sildenafil (16,472 reports, 56.4%)**, tadalafil (11,053 reports, 37.9%), vardenafil (1,159 reports, 4.0%), and avanafil (492 reports, 1.69%)
- **9,979 outcomes** reported among total AEs
  - Most reported outcome: **'other serious medical events' (67.2%), 'hospitalization' (19.5%)**

Figure 1. Most reported adverse events associated with PDE5Is

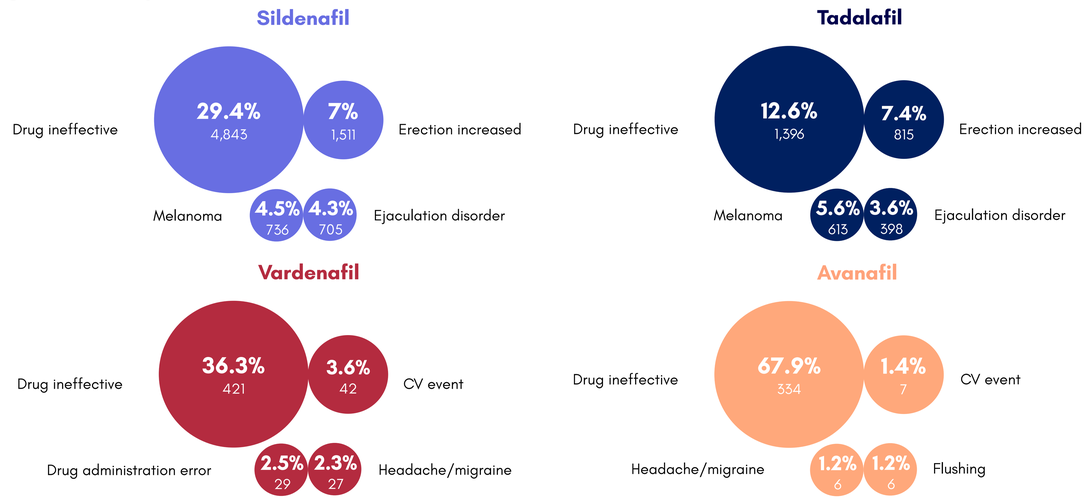
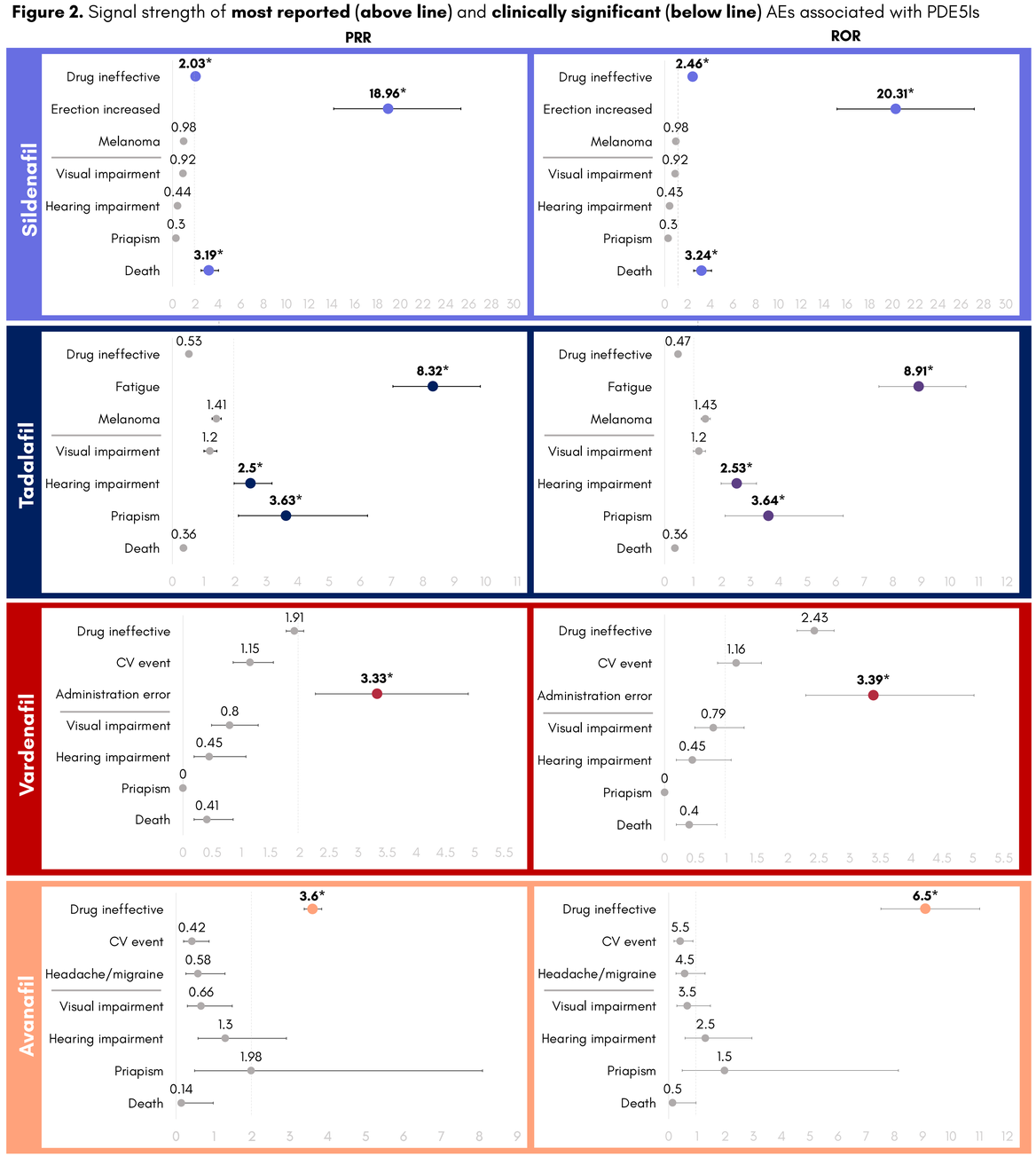


Figure 2. Signal strength of **most reported (above line)** and **clinically significant (below line)** AEs associated with PDE5Is



Note: Colored bubbles indicate positive signals. Asterisks indicate a statistically significant signal.

DISCUSSION

- 1st comprehensive report on all types of AEs associated with PDE5Is
- Most reported AE: '**drug ineffective**'
  - **High discontinuation rates** of PDE5Is due to ineffectiveness or adverse events
- 'Cardiovascular (CV) events'
  - **No excess risk of CV disease or outcomes** in patients with ED treated with PDE5Is[1]
  - Most likely due to **underlying CV disease**
- **Sildenafil & death**
  - Greatest proportion of 'death' outcomes reported among PDE5Is
  - Oldest and most used PDE5Is
  - May be used by larger proportion of patients with comorbidities that have a **significantly increased risk of death**
- **Tadalafil & hearing impairment/loss**
  - **2007 MedWatch alert: sudden decrease in hearing/hearing loss** for sildenafil, tadalafil, vardenafil → **label change**
  - Signal supports the label change
- **Tadalafil & priapism**
  - **Consistent** with study that reported disproportionate reporting for tadalafil[3]
    - Most reports for PDE5Is related to **drugs that cause priapism taken at same time** and/or **inappropriate intake/excessive dosage** (i.e. trazodone, antipsychotics)
  - PDE5Is commonly taken concomitantly with drugs with higher risk of priapism[4]
- **Vardenafil & drug administration error**
  - **Orally disintegrating tablet (ODT)** formulation
  - May be mistaken for regular tablet
  - If purchased through illicit means, patients unlikely to have received proper counseling on administration
- Few studies conducted for above signals – further studies need to confirm signals

LIMITATIONS

- FAERS database: self-reports, duplicate and incomplete reports
  - Incidence can't be estimated
  - Reporting and selection biases
- Causality cannot be established
- Findings should be interpreted cautiously

CONCLUSIONS

- **Significantly increased risks** of reporting **certain clinically important AEs** with PDE5Is
- Further research required to **assess positive signals found**
- Imperative **to continually monitor PDE5I use** at primary care to national surveillance levels to ensure **safe utilization**

DISCLAIMER

This study was supported by Boston Scientific. Siri Rojanasarot is a full-time employee of Boston Scientific. Young Shin is a graduate student at the University of Cincinnati. Ms. Shin is not a Boston Scientific employee; however, she is working on a Global Health Economics and Market Access project with Boston Scientific.

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