



Impact of Phosphodiesterase-5 Inhibitor Use on Overall Survival in Sinonasal Malignancies: A Real-World Database Analysis

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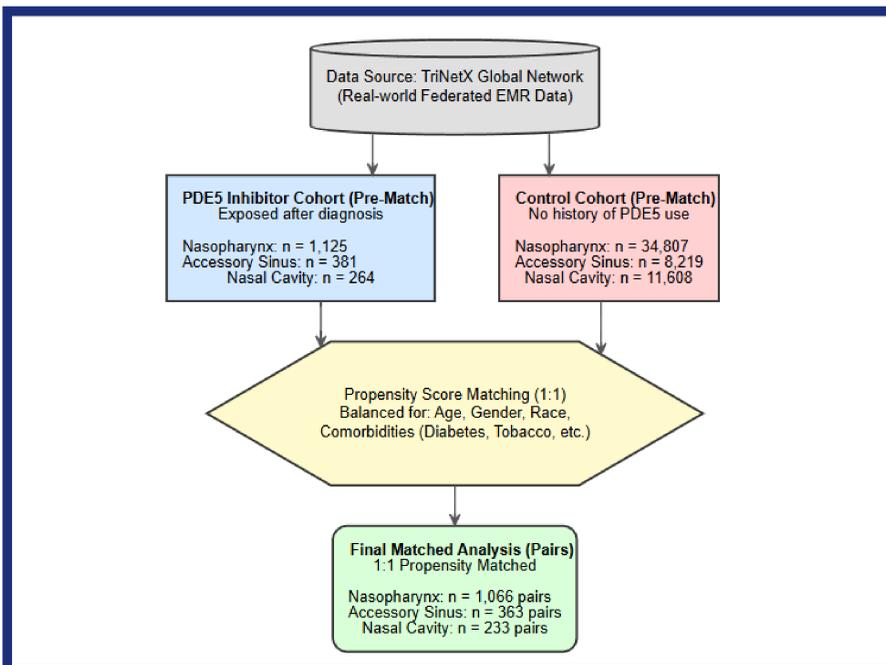
Introduction

- Phosphodiesterase-5 (PDE5) inhibitors (e.g., Sildenafil, Tadalafil) are used for erectile dysfunction but have known immunomodulatory effects.
- PDE5 inhibitors have been shown to suppress Myeloid-Derived Suppressor Cells (MDSCs) and enhance CD8+ T-cell infiltration in the tumor microenvironment.
- While this benefit has been explored in other cancers, data on Sinonasal and Nasopharyngeal malignancies is lacking.

Objective

- To evaluate the association between PDE5 inhibitor usage and 1-year, 3-year, and 5-year Overall Survival (OS) in patients with malignancies of the nasal cavity, nasopharynx, and accessory sinuses using a large, global real-world database.

Methods

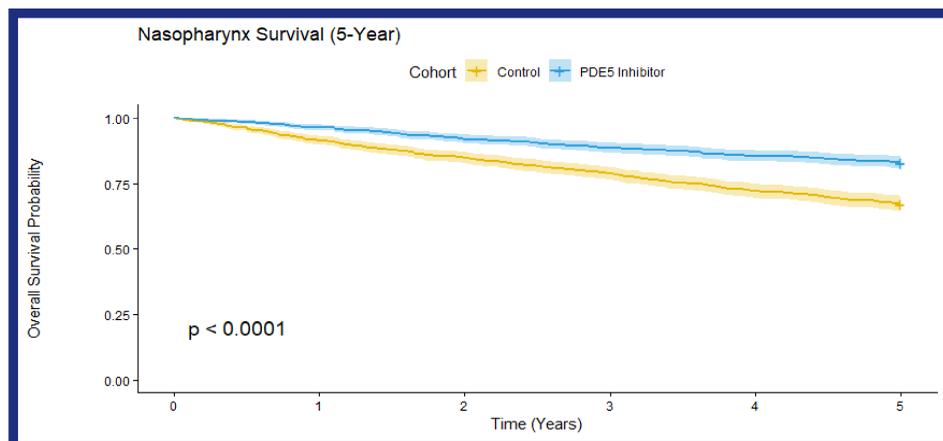
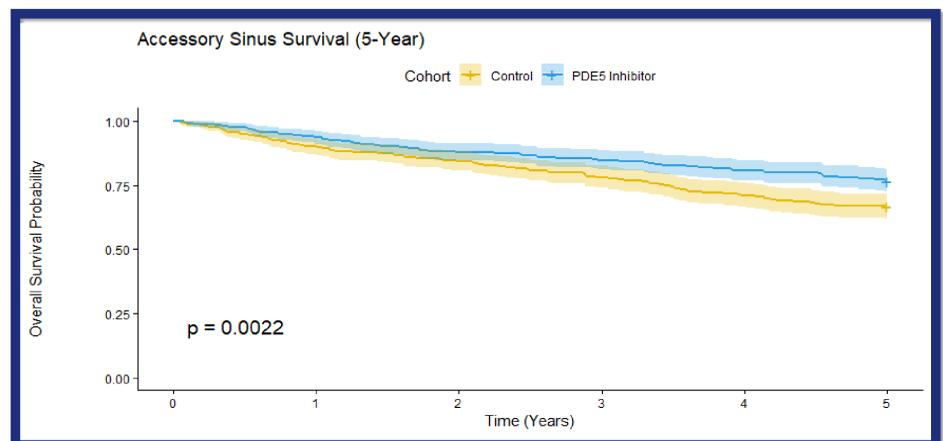
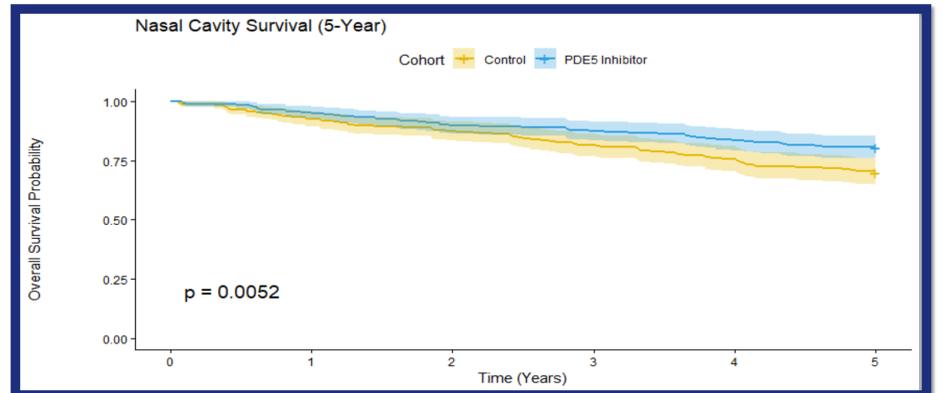


Results

Malignancy	N (Matched Pairs)	1-year OS (PDE5-i vs Control)	3-year OS (PDE5-i vs Control)	5-year OS (PDE5-i vs Control)	5-year HR (95% CI)
Nasopharynx	1,066	94.25% vs 83.36% (p<0.001)	87.15% vs 71.90% (p<0.001)	82.58% vs 65.66% (p<0.001)	0.433 (0.355, 0.527)
Accessory Sinus	363	89.50% vs 83.98% (p=0.046)	81.51% vs 68.99% (p=0.001)	75.14% vs 63.74% (p=0.002)	0.626 (0.462, 0.848)
Nasal Cavity	264	93.67% vs 87.58% (p=0.020)	85.92% vs 72.42% (p=0.001)	77.24% vs 67.61% (p=0.005)	0.555 (0.366, 0.843)

Discussion

- These real-world findings support the mechanistic hypothesis that PDE5 inhibitors may reduce tumor-induced immunosuppression (via MDSC downregulation).
- PDE5 inhibitors are generic, widely available, and have a well-established safety profile, making them ideal candidates for drug repurposing.
- Given the limited treatment options for advanced sinonasal malignancies, this identifies a potential novel adjuvant therapy.
- Retrospective nature (can establish association, not causation), potential residual confounding (e.g., patients on PDE5s might be healthier overall/sexually active, though PSM attempts to control for this).
- Prospective clinical trials are warranted to confirm these benefits.



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