# Hereditary and Clinical Insights into Paraganglioma and Pheochromocytoma

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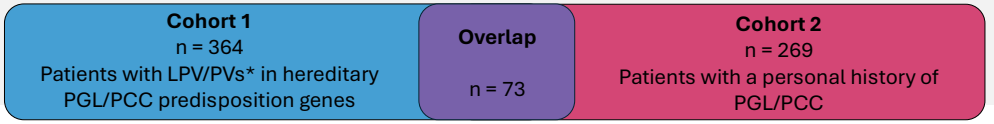
## BACKGROUND

- ~30-40% of paragangliomas (PGL) and pheochromocytomas (PCC) have an underlying hereditary cause.
- Early identification of at-risk individuals is imperative given the early age of onset, aggressiveness of tumors, and other tumor/cancer risks associated with hereditary PGL/PCC.
- Clinical presentations and genetic histories of patients with PGL/PCC and/or hereditary risk were analyzed.

## METHODS

- Retrospective chart review identified two cohorts of patients seen in the cancer genetics clinics between Aug. 2016 and Dec. 2022.
- Demographics, personal and family history, and genetic testing outcomes were analyzed.




*LPV/PVs: likely pathogenic/ pathogenic variants

## RESULTS

| Total (n) | 364 |
|---|---|
| **Age at Date of Service (years), mean ± SD** | **45.6 ± 15.8** |
| **PGL/PCC Gene Positive** | **n (%)** |
| *MAX* | 1 (0.3) |
| *RET* | 53 (14.6) |
| *SDHA* | 36 (9.9) |
| *SDHAF2* | 2 (0.6) |
| *SDHB* | 62 (17.0) |
| *SDHC* | 18 (5.0) |
| *SDHD* | 39 (10.7) |
| *TMEM127* | 6 (1.6) |
| *VHL* | 41 (11.3) |
| *EGLN1* | 0 (0.0) |
| *FH* | 48 (13.2) |
| *KIF1B* | 0 (0.0) |
| *MEN1* | 17 (4.7) |
| *NF1* | 41 (11.3) |

**Table 1:** Cohort 1's gene positive results. 5% of patients also tested positive for LPV/PVs in other hereditary cancer genes.

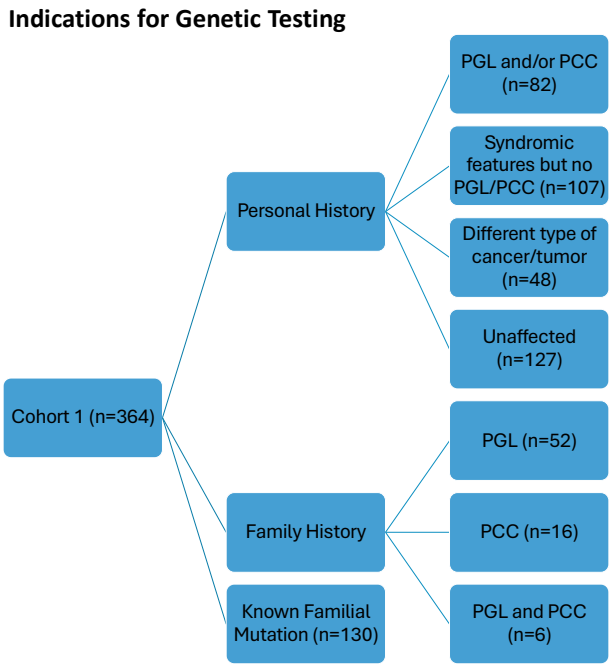



**Figure 1:** The personal and family histories of patients with LPV/PVs in PGL and PCC predisposition genes.

| Total (n) | 269 |
|---|---|
| **Age at Date of Service (years), mean ± SD** | **53.7 ± 15.4** |
| **Age at First PGL/PCC (years), mean ± SD** | **49.4 ± 17.0** |
| **Tumor Presentation** | **n (%)** |
| Single PGL | 153 (56.9) |
| Multiple PGLs | 27 (10.0) |
| Single PCC | 82 (30.5) |
| Multiple PCCs | 5 (1.9) |
| PGL and PCC | 2 (0.7) |
| **Family History of PGL** | **n (%)** |
| Yes | 26 (9.7) |
| No | 243 (90.3) |
| **Family History of PCC** | **n (%)** |
| Yes | 12 (4.5) |
| No | 257 (95.5) |
| **Known Familial Mutation** | **n (%)** |
| Yes | 10 (3.7) |
| No | 259 (96.3) |

**Table 2:** Demographics for patients in Cohort 2.

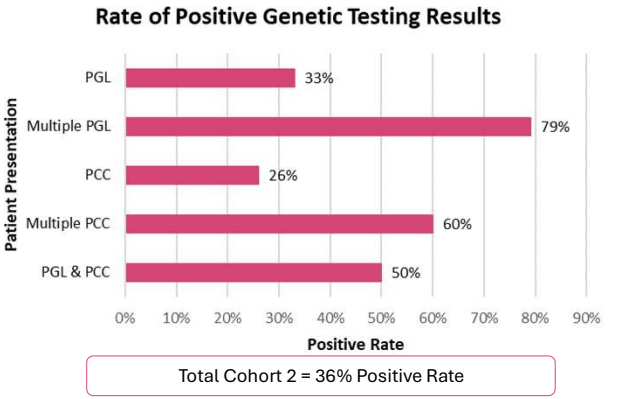



**Figure 2:** Positive rates for patients with single or multiple PGL and/or PCC.

| Cancer | Total | *FH* | *MEN1* | *NF1* | *RET* | *SDHA* | *SDHB* | *SDHC* | *SDHD* | *TMEM 127* | *VHL* |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Breast | 24 | 2 | 2 | 7 | 1 | 2 | 5 | 0 | 3 | 2 | 0 |
| Colon | 2 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Uterus | 2 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 |
| Ovary | 2 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| Pancreas | 2 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 1 |
| Prostate | 5 | 1 | 0 | 0 | 1 | 3 | 0 | 0 | 0 | 0 | 0 |
| None | 37 | 7 | 2 | 5 | 2 | 10 | 2 | 2 | 2 | 3 | 2 |

**Table 3:** The prevalence of LPV/PVs in PGL/PCC genes in patients with select cancers without a personal history of PGL/PCC.

## CONCLUSIONS

- In the era of multigene panel testing, more patients are being identified with hereditary risks for PGL/PCC. However, this also means that more patients are being identified with incidental LPV/PVs findings in PGL/PCC genes.
- Patients presenting with PGL/PCC demonstrate a positive rate of 36%. Patients with multiple PGL or PCC have a higher likelihood of harboring LPV/PVs.
- There is a need for longitudinal studies to better characterize the prevalence and penetrance of these tumors and LPV/PVs across a diverse patient population.

## PUBLICATION

Mauer Hall CB, Watson EM, Prasad T, Myers CL, & Mersch JA. (2024). Hereditary and clinical insights into paraganglioma and pheochromocytoma. *Endocrine Oncology*, *4*(1), e240029.