

Supplemental Results S3. Assessing differences in genetic diagnosis prevalence over the three time periods of our program.

Table SR3-1. Assessing prevalence of genetic diagnosis prevalence over time periods of the clinical program. When restricting the trend analysis to each ECA status respectively, only ECA-negative patients had incremental increases in genetic diagnoses identified over time ($p=0.0015$). These gains were not seen in the ECA-positive patients. Overall, the composite X^2 test adjusting for ECA status showed that there was a potential difference across time, though it was marginally significant ($p=0.0494$).

| marginally significant (p = 0.0494). | | | | |
|--|----------------------|-----------------------|----------------------|-----------------------|
| Time Period | ECA-Negative | | ECA-positive | |
| | Genetic Diagnosis No | Genetic Diagnosis Yes | Genetic Diagnosis No | Genetic Diagnosis Yes |
| | | | | |
| 2014-2018 | 180/195 (92.3%) | 15/195 (7.7%) | 76/118 (64.4%) | 42/118 (35.6%) |
| 2019-2022 | 265/314 (84.4%) | 49/314 (15.6%) | 142/235 (60.4%) | 93/235 (39.6%) |
| 2023 | 57/71 (80.3%) | 14/71 (19.7%) | 49/80 (61.3%) | 31/80 (38.8%) |
| Cochran-Armitage Trend Test one-sided p-value | p=0.0015 | | p=0.2954 | |
| Cochran-Mantel-Haenszel X ² test, controlling for ECA status | p=0.0494 | | | |

Table SR3-2. Assessing prevalence of cytogenetic vs. molecular genetic diagnosis types over time periods of the clinical program. When restricting the trend analysis to each ECA status respectively, only ECA-negative patients had incremental increases in genetic diagnoses identified over time ($p=0.0356$). These gains were not seen in the ECA-positive patients. Overall, the composite X^2 test adjusting for ECA status showed that there was a difference across time ($p=0.0087$).

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|--|-----------------------|-----------------------------|-----------------------|-----------------------------|
| | ECA-Negative | | ECA-positive | |
| | Cytogenetic Diagnosis | Molecular Genetic Diagnosis | Cytogenetic Diagnosis | Molecular Genetic Diagnosis |
| | | | | |
| 2014-2018 | 14/15 (93.3%) | 1/15 (6.7%) | 33/39 (84.6%) | 6/39 (15.4%) |
| 2019-2022 | 34/48 (70.8%) | 14/48 (29.2%) | 57/92 (62.0%) | 35/92 (38.0%) |
| 2023 | 9/14 (64.3%) | 5/14 (35.7%) | 21/30 (70.0%) | 9/30 (30.0%) |
| Cochran-Armitage Trend Test one-sided p-value | p=0.0356 | | p=0.0651 | |
| Cochran-Mantel-Haenszel X ² test, controlling for ECA status | p=0.0087 | | | |