

# Nationwide Implementation and Evaluation of the Tumor-First Workflow for Genetic Testing in Ovarian Carcinoma

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**Background:** Despite international agreement on the importance of tumor DNA testing and germline testing for determining PARP inhibitor treatment eligibility in patients with ovarian carcinoma (OC) and for cancer prevention in their relatives, the optimal strategy remains under debate. In the Netherlands, the “Tumor-First workflow” was initiated and implemented nationwide: a well-validated tumor DNA test is the primary test for detecting tumor pathogenic variants (PVs) in OC risk genes (*BRCA1/2*, *RAD51C/D*, *BRIP1*, *PALB2*). The detection of tumor PVs is subsequently used to stratify germline testing and determine treatment eligibility. The Tumor-First workflow is efficient and saves costs. We evaluated the nationwide implementation of the Tumor-First workflow.

**Methods:** We analyzed real-time genetic testing practices, including tumor DNA and germline testing, in patients diagnosed with OC from 2019 to 2023, as identified through the Dutch Pathology Registry (Palga). Testing data were collected from diagnostic pathology and genetic reports.

**Results:** Out of the 3,926 OC patients, 2,778 (71%) received OC tumor DNA testing as primary test. Between 2019 and 2023, this percentage increased from 50% to 85%. Of these tumor DNA tests, 2,703 (97%) were successful, with 398 (15%) resulting in the identification of a PV in an OC risk gene. Most of these patients (291; 73%) underwent germline testing, and 147 (51%) were found to have a germline PV.

**Conclusion(s):** Nationwide implementation of the Tumor-First workflow for OC was effective. Multidisciplinary efforts contributed to a more efficient detection of germline and somatic PVs in OC risk genes.