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Combining circulating tumor cell and circulating cell-free DNA analyses broadens clinical applicability of liquid biopsy in high grade serous tubo-ovarian carcinoma

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Abstract
Liquid biopsy is a promising strategy for detecting and monitoring neoplastic diseases, with circulating tumor cells (CTCs) and circulating tumor DNA (ctDNA) being the most common objects of investigation. Studies are mainly focusing on these biomarkers separately, and simultaneous detection has never been attempted in high grade serous tubo-ovarian carcinoma (HGSOC). Here, we assess whether tandem CTC/ctDNA analysis improves the efficiency of detecting HGSOC via peripheral blood liquid biopsy. For CTC identification, gene expression assays and *TP53* next-generation sequencing (NGS) were tested using healthy donor samples spiked with known cancer cell numbers. Both approaches detected as few as five spiked cancer cells, showing high analytical sensitivity and specificity. Validation in HGSOC patients and healthy controls revealed better performance of *TP53* NGS, as it correctly identified the disease in 47% liquid biopsies, compared to 13% sensitivity obtained by gene expression assay. *TP53* NGS was also applied for ctDNA detection, where analytical validity was ensured by calculating 0.31% as the optimal variant allele frequency threshold for mutation calling. Clinical validation demonstrated that ctDNA approach, with sensitivity of 70%, outperformed CTC-based methods. Combining ctDNA/CTC analysis improved disease detection rate in two HGSOC cohorts, achieving, respectively, 73.3% and 93.3% sensitivity, which would translate to an absolute gain of additional 13 patients per 100 cases being detected if combined approach is applied compared to ctDNA method alone. Interestingly, we found private CTC variants, and shared ctDNA/CTC mutations undetected in solid biopsy, highlighting the ability of dual-analyte approach to capture tumor heterogeneity and allow mutation cross-validation, which is particularly useful in contexts when solid biopsy is not available. Our study reveals the complementary value of simultaneous ctDNA/CTC analysis in HGSOC, advancing the translational potential of liquid biopsy integration for management of this disease, especially regarding early detection, chemotherapy response evaluation and relapse detection.

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Keywords Liquid biopsy, High grade serous tubo-ovarian carcinoma, Circulating tumor cells, Circulating tumor DNA, *TP53* genotyping

To the Editor,

Improving liquid biopsy in high-grade serous tubo-ovarian carcinoma (HGSOC) is a cogent need, since no screening protocols are available and 80% of cases are diagnosed late, when 5-year survival rates drop to 32% [1]. With current liquid biopsy workflows in this disease being still explorative [2], we here for the first time provide data suggesting dual analyte assessment of circulating tumor cells (CTCs) and circulating cell-free tumor DNA (ctDNA) may improve HGSOC detection rate in peripheral blood (PB) and increase the confidence of liquid biopsy results when solid biopsy is not available.

Assays for both analytes were first optimized and then validated in HGSOC and control cohorts (Fig.S1, Tab. S1). For CTCs, Parsortix and CD45-negative enrichment were compared, along with gene expression and Next Generation Sequencing (NGS) detection assays (Fig. 1A). To establish analytical validity, mock liquid biopsies were generated by spiking healthy donor PB with known numbers of SKOV3^{GFP} cells, which also enabled tracking during isolation (Fig. 1B). For gene expression profiling, HGSOC CTC-associated genes were retrieved from the literature (Tab.S2), and their analytical validation revealed *AGR2*, *GPX8* and *WT1* as specific liquid biopsy markers (Fig. 1C–E). The latter were detected in all spiked samples when we used preamplification-based quantitative Real-Time PCR (qRT-PCR), demonstrating its higher sensitivity compared to digital PCR, which failed to recognize the transcripts in samples carrying five SKOV3^{GFP} (Fig. 1F, Fig.S2). Interestingly, NGS has never been implemented for CTC detection in HGSOC. Thus, we explored the analytical validity of Ion AmpliSeq HD laboratory-developed panel for screening *TP53*, tumor suppressor mutated in virtually all HGSOCs [3]. Since comparable CTC recovery was observed between Parsortix and CD45-negative sorting (Fig. 1F), the former was used due to marker agnostic methodology and CTC cluster capture ability. In all spiked mock liquid biopsies, *TP53* NGS revealed exclusively the SKOV3 c.267delC mutation (Fig. 1G), ensuring high analytical sensitivity and specificity of the assay. Next, we evaluated clinical validity of both gene expression and NGS approaches comparing HGSOC and healthy donor liquid biopsies (Fig. 1H). Gene expression assay identified only two out of 15 HGSOC cases (13%), whereas *TP53* NGS retrieved 15 mutations in seven out of 15 patients (47%), revealing its superior sensitivity (Fig. 1I–J, Tab.S3).

TP53 NGS was implemented also for ctDNA detection, since previously resulted promising in HGSOC setting [4]. However, caution is required when dealing with ctDNA *TP53* variants due to possible false positives [5, 6], mainly accounted to clonal hematopoiesis (CH)-associated mutations [7]. Thus, to ensure analytical validity, we first determined the variant allele frequency (VAF) threshold for optimal mutation calling (Fig. 1K). Circulating cell-free DNA (cfDNA) was sequenced in 20 HGSOCs and resulting variants were validated in matched primary tumor tissue to discriminate between tumor confirmed and cfDNA private variants (Fig.S3). Then, the VAF value of each variant was associated with positive (tumor confirmed) or negative (cfDNA only) category to build Receiver Operating Curve (ROC) (Fig. 1L). Youden's J factor across different VAFs highlighted 0.31% as the optimal cut-off (Fig. 1L), which was additionally confirmed by Leave-One-Out Cross-Validation (LOOCV) (Fig. 1M). The identified value is higher compared to thresholds applied in similar studies, which defined the cut-off based on technical limit of detection rather than by performing analytical validation [8, 9]. Next, to assess clinical validity of the approach (Fig. 1N), liquid biopsies of 30 HGSOC (Fig.S1) were compared to those from six low-grade serous ovarian cancer (LGSOC) patients (Tab.S1), as the latter represent the optimal negative controls carrying high cfDNA abundance due to tumor burden (Fig. 1O), but lack *TP53* mutations [10]. Twenty-seven *TP53* variants were identified in 21 HGSOC patients (70%) (Fig. 1P, Tab.S4), whereas none were found among LGSOC liquid biopsies (Fig. 1Q). Our results imply the specificity of the assay is high, but further studies of independent cohorts are required to ascertain clinical robustness of the 0.31% threshold. Overall, ctDNA identification outperformed CTC-based approaches in detecting HGSOC.

Finally, we compared the data obtained by CTC and ctDNA based assays. In cohort 1, we observed concordant negativity in four cases (27%), and no concordant positivity, with two patients positive exclusively for CTCs (13%), and nine for ctDNA only (60%) (Fig. 2A). The disease detection rate increased from 60% when ctDNA alone was considered, to 73% when also CTC identification was included (Fig. 2B), showing that the combinatory approach holds potential for improving the clinical utility of PB liquid biopsy for HGSOC. This finding was confirmed in cohort 2, where one case displayed concordant negativity (7%), five concordant positivity (33%), with two patients being positive exclusively for CTCs (13%) and seven exclusively for ctDNA (47%) (Fig. 2C). In cohort 2, the combinatory approach increased disease detection sensitivity to 93%, compared to 47% and 80% obtained by CTC or ctDNA alone, respectively (Fig. 2D).

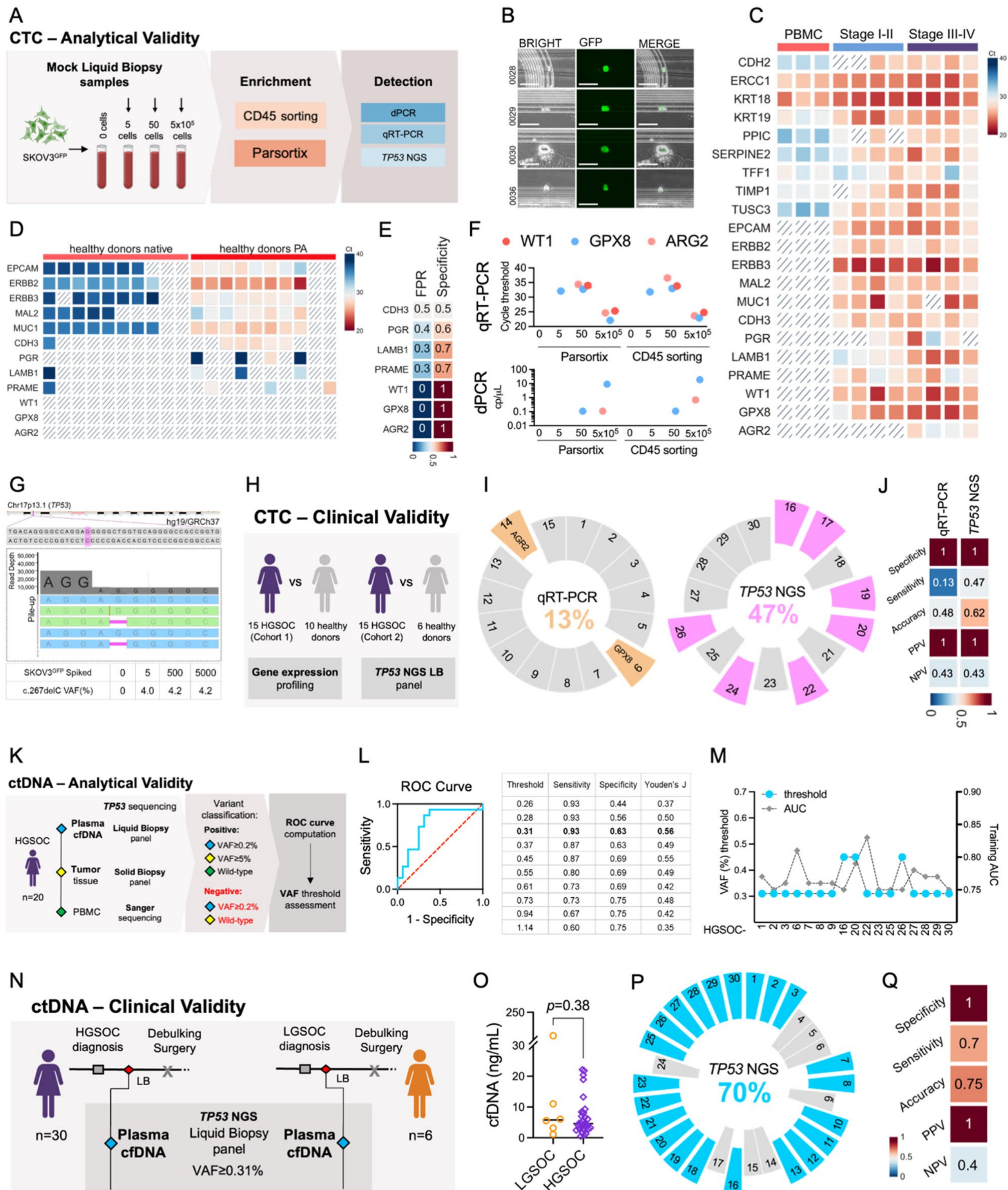

Fig. 1 (See legend on next page.)

Results from both cohorts concur that the effect-size of sensitivity improvement when applying combined approach, compared to the ctDNA method alone, translates in an absolute gain of additional 13 patients per 100 cases being detected (relative improvement of 22% for cohort 1 and 16.3% for cohort 2). From a clinical utility point of view, this may potentially represent a significant reduction in the number of missed cases. Of note,

(See figure on previous page.)

Fig. 1 Analytical and clinical validity assessment of CTC- and ctDNA-based assays for detection of HGSOC in patient liquid biopsies. **A** Graphical sketch of the experimental workflow designed to compare CTC enrichment and detection methods by using mock liquid biopsy samples. **B** Images of SKOV3^{GFP} captured by Parsortix cassette after processing healthy donor PB spiked with five cells. Brightfield (BRIGHT), GFP, and merged channels are shown in four fields of view in which GFP signal was observed (0028, 0029, 0030 and 0036). Scale bar = 100 µm. **C** Cycle-threshold (Ct) heatmap obtained via qRT-PCR of RNA extracted from three healthy donor PBMCs and eight primary tumors biopsies from HGSOC patients (Tab.S1). Slashed boxes indicate undetected transcripts. **D** Ct heatmap obtained via qRT-PCR of RNA extracted from PBMCs of ten healthy donors with native or preamplifed (PA) cDNA. Slashed boxes indicate undetected transcripts. **E** Heatmap reporting false positive rate (FPR) and specificity values calculated for each gene. **F** Dot plots reporting Cts or cDNA concentrations obtained by, respectively, preamplification/qRT-PCR or digital PCR (dPCR). Samples derived from healthy donor PB samples spiked with 0, 5, 50 and 500'000 SKOV3^{GFP} cells and enriched with either Parsortix or CD45-negative sorting. **G** Representative *TP53* NGS GenomeBrowser output image of the sample spiked with five SKOV3^{GFP} cells. The pink bar indicates c.267delC mutation locus, with blue and green bars indicating complementary sequencing reads. y-axis reports read depth. The adjacent table lists *TP53* c.267delC VAFs. **H** Graphical sketch of the experimental workflow designed to assess clinical validity of CTC-based methods for HGSOC detection. For gene expression profiling, 15 HGSOCs (cohort 1) and 10 healthy donors were used, respectively, as positive and negative reference groups. For *TP53* NGS, 15 HGSOCs (cohort 2) and 6 healthy donors were used, respectively, as positive and negative reference groups. **I** Pie charts reporting the disease detection rates obtained in HGSOC patient liquid biopsies by either gene expression (qRT-PCR) in cohort 1 or *TP53* NGS in cohort 2. **J** Heatmaps reporting the performance metrics of gene expression (qRT-PCR) or *TP53* NGS in detecting HGSOC via CTC-based PB liquid biopsy, by using patient and healthy donor samples described in Fig. 1H, Fig.S1 and Tab.S1. 95% Confidence intervals (CI) for sensitivity and specificity are, respectively, 3.7–37.9% and 72.2–100% for qRT-PCR (Fisher's exact test $p=0.5$); and 24.8–69.9% and 61–100% for *TP53* NGS (Fisher's exact test $p=0.06$). PPV-positive predictive value; NPV-negative predictive value. **K** Graphical sketch of the workflow for ensuring analytical validity of *TP53* NGS ctDNA detection. cfDNA was sequenced in 20 HGSOCs and resulting variants were validated in matched primary tumor tissue to discriminate between tumor confirmed and cfDNA private variants. PBMC was sequenced to confirm somatic nature of the former. To define ctDNA detection VAF cut-off, ROC curve was built by associating the VAF values of each variant with the positive or negative category, considering the solid biopsy confirmed variants as positive, while the remaining cfDNA private variants as negative. **L** ROC curve (blue) with respective sensitivity, specificity, and Youden's J values calculated for each VAF threshold. The area under the curve (AUC) is 0.77 (SE ± 0.02), with 95% CI of 0.58–0.95 (Permutation test $p=0.01$, Hanley-McNeil Z-test $p=0.002$). Dashed red line indicates the random classifier. The optimal cut-off value is indicated in bold in the adjacent table. **M** Dot-plot reporting the LOOCV for VAF threshold (blue) and AUC (gray). x-axis indicates the HGSOC patient used for iteration. **N** Graphical sketch of the workflow for clinical validity assessment of ctDNA detection via *TP53* NGS. HGSOC ($N=30$, Fig.S1) and LGSOC ($N=6$, Tab.S1) liquid biopsies (LB) were used as positive and negative controls, respectively. **O** Median plasma cfDNA concentration in LGSOC (orange) and HGSOC (purple) patients. Single dots represent patients and black bars the median values. p value indicates t-test result. **P** Pie chart reporting the disease detection rate obtained in HGSOC patient liquid biopsies by cfDNA *TP53* NGS. **Q** Heatmap reporting the performance metrics of *TP53* NGS ctDNA detection assay, by using HGSOC and LGSOC samples described in Fig. 1N, Fig.S1 and Tab.S1. 95% CIs for sensitivity and specificity are, respectively, 54.8–93% and 61–100% (Fisher's exact test $p=0.002$). PPV-positive predictive value; NPV-negative predictive value

generally higher sensitivity obtained by liquid biopsy in cohort 2 may be explained by the larger proportion of chemotherapy naïve patients in this group (Fig. S1), as they usually exhibit higher *TP53* mutation detection rates [11]. Intriguingly, *TP53* sequencing of both analytes revealed shared ctDNA/CTC mutations undetected in solid tumor biopsy in 20% of patients, as well as private CTC variants in 40% of cases (Fig. 2E–F). Further studies are warranted to provide biological explanations for this finding, possibly by including parallel single cell sequencing of the primary/metastatic tumors and pure CTC isolation rather than enrichment. Although unexpected, we cannot but report the ctDNA/CTC private variants as disease-associated since they were not detected by sequencing available matched PBMCs (Fig. 2E), which the European Liquid Biopsy Society guidelines indicate as the only means to exclude CH-related events [12]. Moreover, no unspecific variants were detected in negative controls used for analytical and clinical validity estimation, neither in the spiked samples (Fig. 1G), nor in age-matched healthy donors (Fig. 1H–J) or LGSOC liquid biopsies (Fig. 1N–Q), demonstrating that the applied NGS method is not prone to technical errors. These data suggest dual-analyte approach may allow variant cross-validation, increasing the confidence of liquid biopsy results, and improve capturing of HGSOC genetic heterogeneity, which is in concordance with studies combining ctDNA/CTC analysis in other cancers, generally agreeing that considering both analytes broadens clinical applicability of liquid biopsy [13, 14]. Evaluating whether both CTCs and ctDNA are useful in contexts when solid biopsy is not available may be appropriate, such as during minimal residual disease assessment. Moreover, it might also improve HGSOC staging or genetic profiling for therapeutic decisions via analyses of ascites, as the latter is emerging as a less invasive alternative to tumor sampling [15, 16].

Overall, our seminal findings represent a step forward in advancing PB liquid biopsy for HGSOC by demonstrating that, while cfDNA analysis outperforms CTC-based assays, their combination may increase the translational value of the approach. We acknowledge that reported sensitivities are derived from relatively small cohorts. Independent validation in larger patient and control populations is warranted to reveal the full clinical applicability of this dual-analyte strategy. Future studies may envision including other liquid biopsy analytes such as exosomes, as well as fluids beyond blood [17], to eventually allow earlier diagnosis, more accurate minimal residual disease evaluations, optimal therapeutic

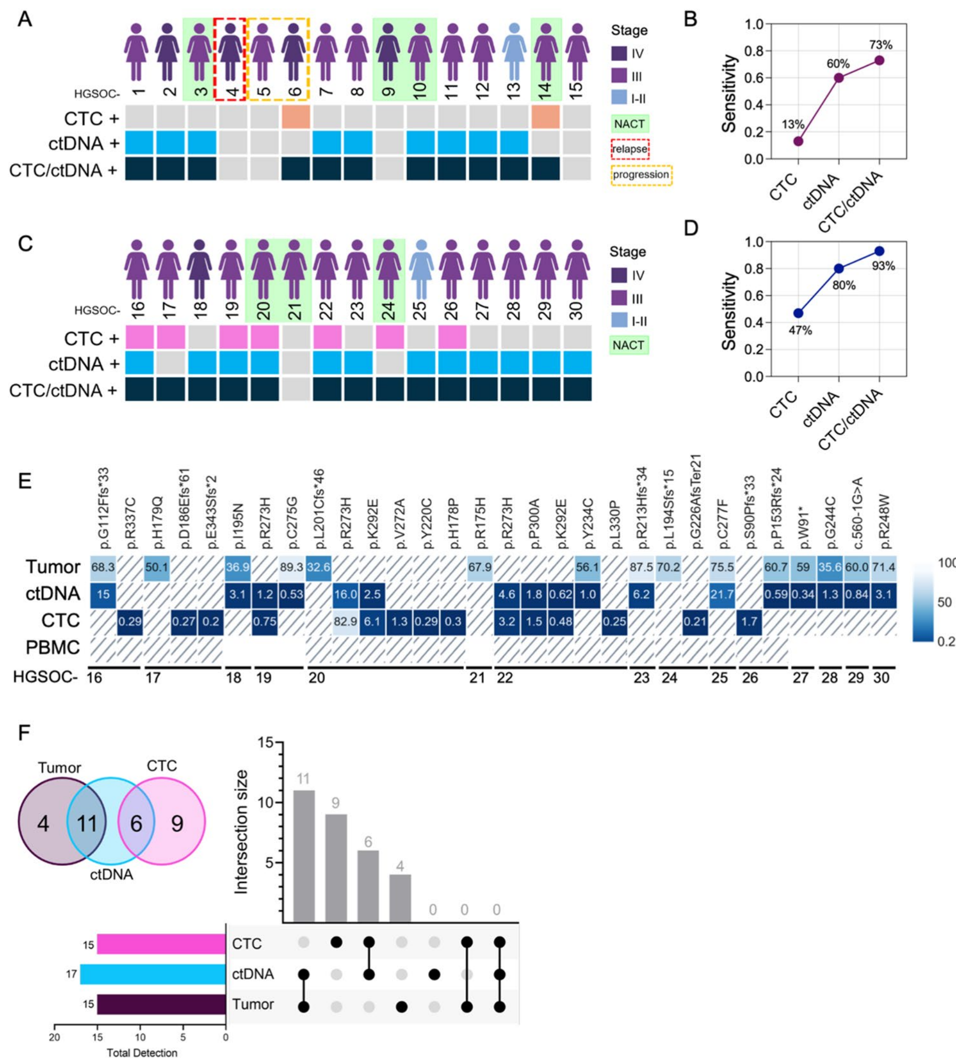

Fig. 2 Combining CTC and ctDNA detection in HGSOC liquid biopsies. **A** Schematic representation of CTC and ctDNA detection across cohort 1. Colored and gray boxes indicate positive and negative results, respectively. **B** Sensitivity of CTC, ctDNA, and combined detection assays across cohort 1. **C** Schematic representation of CTC and ctDNA detection across cohort2. Colored and gray boxes indicate positive and negative results, respectively. **D** Sensitivity of CTC, ctDNA, and combined detection assays across cohort 2. **E** VAF heatmap of *TP53* mutations identified in solid and liquid biopsies of cohort 2. Slashed boxes indicate wild-type genotype, whereas white boxes represent samples which were not available for the analysis. **F** Venn diagram and UpSet plot showing shared *TP53* variants across the three analytes: solid tumor, ctDNA and CTC. The horizontal bar plot indicates the number of variants found in each analyte, whereas the vertical bar plot shows the number of variants shared between various sample types (Intersection size), according to the black dot intersections found below

choices, and timely anticipation of relapse before radiologic progression.

Abbreviations

cfDNA	Circulating cell-free DNA
CH	Clonal hematopoiesis
CTCs	Circulating tumor cells
ctDNA	Circulating cell-free tumor DNA
HGSOC	High grade serous tubo-ovarian cancer
LOOCV	Leave-one-out cross-validation
LGSOC	Low grade serous ovarian cancer
NGS	Next-generation sequencing
PB	Peripheral blood
PBMC	Peripheral blood mononuclear cell
qRT-PCR	Quantitative real time-PCR
ROC	Receiver operating characteristic
VAF	Variant allele frequency

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s40164-026-00774-4.

Supplementary Material 1.

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Author contributions

Conceptualization, B.C., I.K.; methodology, B.C., D.d.B.; acquisition and analysis, B.C., S.Cor., M.D.L., S.L., C.A.C., G. Gi., S. Col., A.D.L., D.d.B., I.K.; data interpretation: B.C., S.d.C., F.M., P.D.I., A.Ma.P., A.My.P., D.d.B., G.Ga., I.K.; writing – original draft,

B.C., I.K., writing – review & editing, B.C., C.A.C, A.Ma.P., A.My.P., D.d.B., G.Ga, I.K.; project administration, I.K., funding acquisition and resources, A.D.L., A.Ma.P., G.Ga., I.K. All authors have approved the submitted version of the work and have agreed both to be personally accountable for the author's own contributions and to ensure that questions related to the accuracy or integrity of any part of the work, even ones in which the author was not personally involved, are appropriately investigated, resolved, and the resolution documented in the literature.

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Data availability
All data generated and analysed during this study are included in this published article and its Additional file, apart from raw device output data, which are deposited in https://www.ncbi.nlm.nih.gov/bioproject/PRJNA1338131 and https://doi.org/10.6092/unibo/amsacta/8538.

Declarations

Ethics approval and consent to participate
This study was conducted in accordance with the Declaration of Helsinki and the protocol was approved by the Independent Ethics Committee "Comitato Etico di Area Vasta Emilia Centro" (Protocol EM363-2024_107/2011/U/Tess/AOUBo). All subjects enrolled in the study provided written informed consent for their participation.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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References
1. Li T, Zhang H, Lian M, He Q, Lv M, Zhai L, et al. Global status and attributable risk factors of breast, cervical, ovarian, and uterine cancers from 1990 to 2021. J Hematol Oncol. 2025;18:5. https://doi.org/10.1186/s13045-025-01660-y.
2. Asante D-B, Calapre L, Ziman M, Meniawy TM, Gray ES. Liquid biopsy in ovarian cancer using circulating tumor DNA and cells: ready for prime time? Cancer Lett. 2020;468:59–71. https://doi.org/10.1016/j.canlet.2019.10.014.
3. Ahmed AA, Etemadmoghadam D, Temple J, Lynch AG, Riad M, Sharma R, et al. Driver mutations in TP53 are ubiquitous in high grade serous carcinoma of the ovary. J Pathol. 2010;221:49–56. https://doi.org/10.1002/path.2696.
4. Heo J, Kim Y-N, Shin S, Lee K, Lee J-H, Lee YJ, et al. Serial circulating tumor DNA analysis with a tumor-naïve next-generation sequencing panel detects minimal residual disease and predicts outcome in ovarian cancer. Cancer Res. 2024;84:468–78. https://doi.org/10.1158/0008-5472.CAN-23-1429.
5. Magee D, Domenyuk V, Abraham J, Perdigones Borderias N, Swensen J, Solipuram P, et al. Characterization of plasma cell-free DNA variants as of tumor or clonal hematopoiesis origin in 16,812 advanced cancer patients. Clin Cancer Res. 2025. https://doi.org/10.1158/1078-0432.CCR-24-3335.
6. Luo X, Xie S, Hong F, Li X, Wei Y, Zhou Y, et al. From multi-omics to deep learning: advances in cfDNA-based liquid biopsy for multi-cancer screening. Biomark Res. 2025;14:3. https://doi.org/10.1186/s40364-025-00874-z.
7. Hu Y, Ulrich BC, Supplee J, Kuang Y, Lizotte PH, Feeney NB, et al. False-positive plasma genotyping due to clonal hematopoiesis. Clin Cancer Res. 2018;24:4437–43. https://doi.org/10.1158/1078-0432.CCR-18-0143.
8. Calapre L, Giardina T, Beasley AB, Reid AL, Stewart C, Amanuel B, et al. Identification of TP53 mutations in circulating tumour DNA in high grade serous ovarian carcinoma using next generation sequencing technologies. Sci Rep. 2023;13:278. https://doi.org/10.1038/s41598-023-27445-2.
9. Widjaja AO, Micallef P, Lycke M, Österlund T, Santamaría ML, Lindberg JH, et al. Detecting TP53 mutations in paired liquid and tissue biopsies from patients with high-grade serous ovarian carcinoma. Int J Cancer. 2026;158:2043–50. https://doi.org/10.1002/ijc.70277.
10. Matulonis UA, Sood AK, Fallowfield L, Howitt BE, Sehouli J, Karlan BY. Ovarian cancer. Nat Rev Dis Primers. 2016;2:16061. https://doi.org/10.1038/nrdp.2016.61.
11. Zelisse HS, van der Pol Y, Mouliere F, Dijk F, Halfwerk JBG, Mearadji B, et al. Improving cell-free DNA detection in advanced-stage high-grade serous ovarian cancer using combined TP53 mutational status and copy number changes. Pathol Res Pract. 2025;272:156038. https://doi.org/10.1016/j.prp.2025.156038.
12. de Jager VD, Giacomini P, Fairley JA, Toledo RA, Patton SJ, Joosse SA, et al. Reporting of molecular test results from cell-free DNA analyses: expert consensus recommendations from the 2023 European liquid biopsy society ctDNA workshop. EBioMedicine. 2025;114:105636. https://doi.org/10.1016/j.ebiom.2025.105636.
13. Alba-Bernal A, Godoy-Ortiz A, Domínguez-Recio ME, López-López E, Quirós-Ortega ME, Sánchez-Martín V, et al. Increased blood draws for ultrasensitive ctDNA and CTCs detection in early breast cancer patients. NPJ Breast Cancer. 2024;10:36. https://doi.org/10.1038/s41523-024-00642-6.
14. Manier S, Park J, Capelletti M, Bustoros M, Freeman SS, Ha G, et al. Whole-exome sequencing of cell-free DNA and circulating tumor cells in multiple myeloma. Nat Commun. 2018;9:1691. https://doi.org/10.1038/s41467-018-04001-5.
15. Kfoury M, Hazzaz RE, Sanson C, Durand FB, Michels J, Blameble EC, et al. Circulating tumor DNA from ascites as an alternative to tumor sampling for genomic profiling in ovarian cancer patients. Biomark Res. 2023;11:93. https://doi.org/10.1186/s40364-023-00533-1.
16. Kurelac I, Sollazzo M, De Luise M, Nanetti F, Lanteri L, D'Angelo L, et al. Immunomagnetic enrichment coupled to PAX8/TP53 molecular pathology approach increases sensitivity in the detection of ovarian cancer cells in ascites. Front Mol Biosci. 2025;12:1537407. https://doi.org/10.3389/fmolb.2025.1537407.
17. Nikanjam M, Kato S, Kurzrock R. Liquid biopsy: current technology and clinical applications. J Hematol Oncol. 2022;15:131. https://doi.org/10.1186/s13045-022-01351-y.

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