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Original research

Translating ctDNA into cutaneous melanoma care: An international expert survey

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ABSTRACT

Background: Circulating tumor DNA (ctDNA) is a promising biomarker in melanoma, with higher sensitivity for tumor burden detection than conventional diagnostics. While well established in research, clinical routine implementation remains pending. Key global questions concern optimal clinical applications and barriers to adoption.

Methods: A web-based survey of 116 members of the Melanoma World Society Study Group assessed international expert opinions on ctDNA utility across predefined clinical scenarios. The questionnaire included 18 general questions on ctDNA use and 5 clinical vignettes with de-identified patient data and retrospectively obtained ctDNA results.

Results: ctDNA was rated most valuable for detecting minimal residual disease (mean score 3.63), surveillance of recurrent disease (3.85), and stage IV melanoma (3.82), with limited utility in early stages. Experts considered ctDNA superior to S100 and LDH for early relapse detection and identifying progressive disease. Most participants (80%) agreed that ctDNA correlates with radiographic response, and 82% favored its integration into routine follow-ups. In urgent high-tumor-burden settings, 82.8% would initiate BRAFi/MEKi therapy based on ctDNA if tissue analysis was pending, and 93.9% if unavailable. For central nervous system lesions, 62% did not support blood ctDNA, while 66% considered cerebrospinal fluid valuable. Pragmatic approaches with small to mid-size targeted panels and short turnaround times were preferred. Major barriers included the need for prospective trials (85%), standardized guidelines (83%), and reimbursement policies (82%).

Conclusion: Key opinion leaders regarded ctDNA as a valuable adjunct selected melanoma scenarios. Validation through prospective studies, guideline development, and reimbursement frameworks are essential for broader clinical implementation.

1. Introduction

Circulating tumor DNA (ctDNA) has emerged as a promising biomarker in melanoma, enabling the detection of tumor-derived genetic alterations through minimally invasive liquid biopsies [1,2]. Multiple studies have demonstrated that ctDNA can reflect tumor burden, monitor treatment response, and detect minimal residual disease (MRD) or early relapse, often preceding radiographic evidence of progression [3–7]. Nevertheless, ctDNA testing remains confined to research settings and has not yet been established as a routine clinical practice in melanoma care [8].

The discrepancy between accumulating scientific evidence and limited real-world implementation highlights a translational gap. While ctDNA is frequently explored in advanced disease, its potential role in earlier stages of melanoma and in complex clinical scenarios, such as central nervous system (CNS) involvement or ambiguous imaging findings, remains under debate [9–12].

A systematic assessment of expert perspectives is therefore essential to define where ctDNA is already considered clinically meaningful, to clarify the most pressing limitations, and to understand how these perceptions vary across disease stages and scenarios. Surveys targeting melanoma experts can provide valuable insights into the practical considerations, expectations, and perceived gaps that shape the adoption of ctDNA in real-world settings.

Here, we report findings from an international expert survey conducted among members of the Melanoma World Society Study Group. The survey systematically evaluated current opinions on the clinical use of ctDNA across different disease stages and scenarios, identified applications where ctDNA is most beneficial, mapped key hurdles to broader adoption, and explored how experts envision its future integration into melanoma care under ideal conditions of approval and reimbursement.

2. Material and methods

2.1. Study design and survey development

This prospective expert survey used a questionnaire with two sections. The first part included 18 questions that explored experts' current opinions on the use of ctDNA in melanoma. The second part presented five use cases in the form of vignettes, designed to elicit clinical perspectives on the benefits and applications of ctDNA in realistic settings. The clinical scenarios were representative of the cutaneous melanoma spectrum across different disease stages. Rare melanoma subtypes, such as acral, mucosal or uveal melanoma, were not specifically addressed. The vignettes were constructed using de-identified patient data from patients who presented at the Skin Cancer Center of the University Medical Center Hamburg-Eppendorf, including medical history (age group, primary tumor characteristics, American Joint Committee on Cancer version 8 [AJCC-v8] stage, metastatic status), prior and ongoing systemic treatments, and biomarker levels (S100, LDH). Each vignette reflected a real tumor board situation and was accompanied by retrospectively acquired ctDNA results to assess the perceived clinical impact. Case-sensitive and general follow-up questions complemented each vignette. The full survey instrument, including the exact wording of all general and vignette-specific questions, is provided in the Supplementary Material (Supplementary File 1).

Survey items were structured using predefined response formats to ensure consistency across participants. Perceived clinical value was assessed using a Likert-type scale ranging from 0 (not valuable) to 5 (very valuable). Questions addressing reliability, correlation with radiographic response, or superiority compared to established biomarkers (S100 and LDH) were structured as categorical responses (Yes/No/Unsure). "Involvement" in ctDNA use was defined through direct questions regarding (i) the application of ctDNA in clinical decision-making and (ii) participation in ctDNA-related clinical or translational research.

Preferences regarding ctDNA testing strategies (including panel size, turnaround time, and cost considerations) were assessed using predefined implementation scenarios. The predefined testing scenarios included differences in panel size, analytical platform, requirement for tumor material, turnaround time, site of analysis, mutational coverage,

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and relative cost. Relative cost categories (e.g., lowest, medium, high, highest) were presented descriptively as part of these structured options and were not intended to reflect absolute pricing, reimbursement policies, or formal health economic evaluation.

The survey was web-based and distributed exclusively to members of the Melanoma World Society Study Group. Participation was voluntary and anonymous. The survey was conducted between June and August 2025. Of the 300 invited colleagues, 116 completed the questionnaire (38.7 %). Only fully completed submissions were included in the final analysis.

2.2. Patient selection and data preparation for vignettes

Five patient cases from the Department of Dermatology and Venereology were retrospectively selected from the institutional biobank at University Medical Center Hamburg-Eppendorf. Selection was based on the following criteria: (a) Patients consented to the institutional biobank and were discussed in the local tumor board. (b) Presence of a tumor mutation detectable with the Oncobit PM platform (Oncobit, Zurich, Switzerland), which had previously been identified from routine pathological examination (no explicit testing of the presence of mutations in tumor tissue was conducted for this project). (c) Availability of biobank plasma samples, which had been collected at the time of tumor board presentation. Patients without a detectable mutation on the Oncobit PM platform or without adequate plasma samples for ctDNA analysis were excluded. Clinical situations represented in the questionnaire included: (1) unknown *BRAF* mutation status, (2) MRD detection, (3) unclear routine diagnostic findings, (4) CNS lesions, and (5) therapeutic switch between targeted and immunotherapy (Supplementary material p. 10–15). Patient datasets were correlated with ctDNA results in double-pseudonymized form. Data were fully anonymized for survey use, in compliance with local ethical regulations.

2.3. ctDNA analysis

Cell-free DNA was isolated from plasma using the NucleoSnap cfDNA

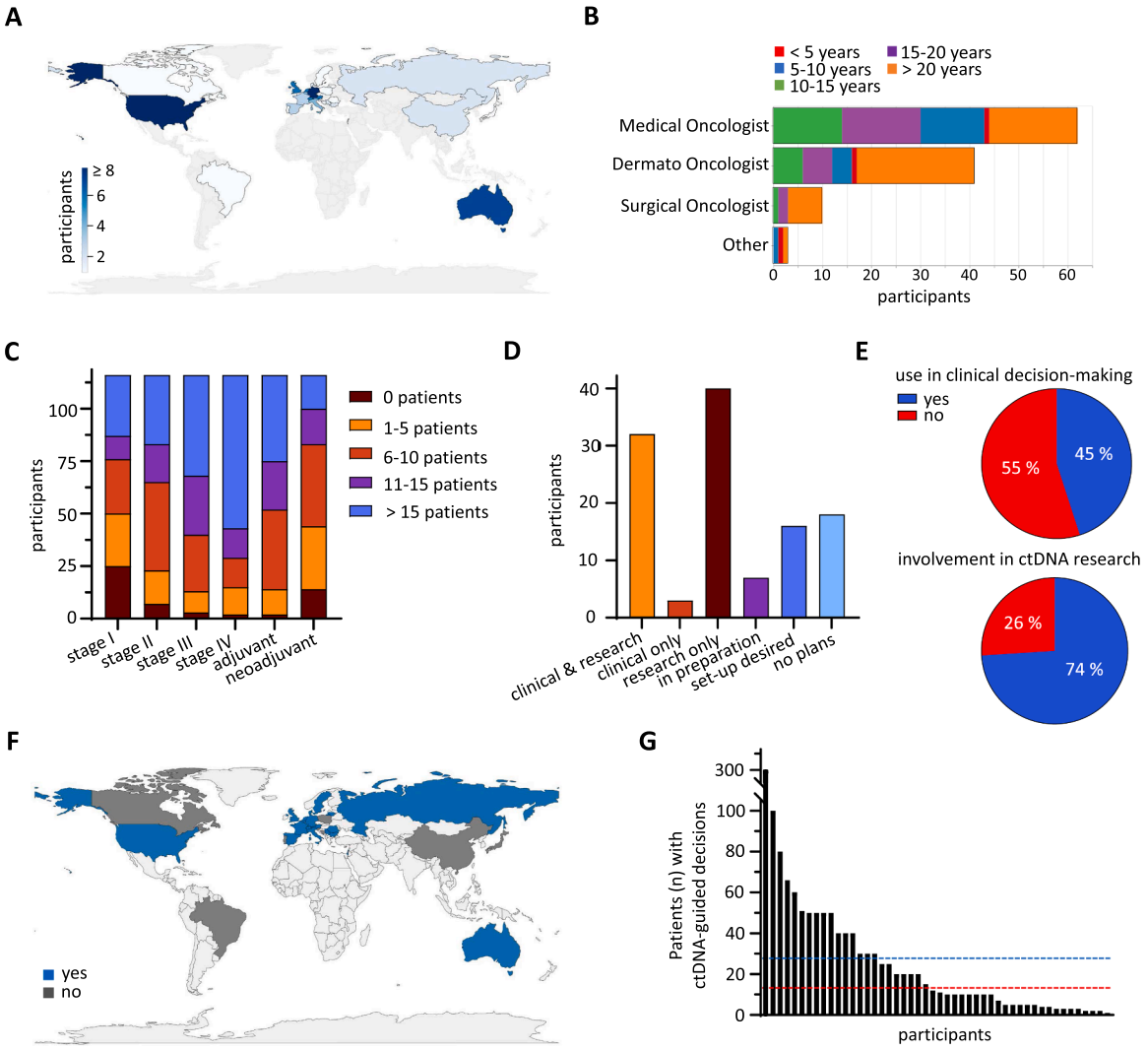

Fig. 1. Cohort profiles and current institutional practices regarding ctDNA in melanoma. (A) Geographic distribution of survey participants, displaying the number of participants per country on a colored scale. Countries without participants are depicted in gray. (B) Professional background and years of experience in melanoma care. (C) Number of melanoma patient cases per month that participants are seeing in their practice or clinic, categorized by disease stage and treatment setting. (D) Current implementation status of ctDNA measurements at participants' centers, differentiating clinical, research, preparatory use, plans of set-up, and no plans of establishment. (E) Proportion of participants who have been using ctDNA results in clinical decision-making (top) and those involved in ctDNA-related research (bottom). (F) Countries reporting clinical use of ctDNA in blue versus no current use in dark grey. Counties not represented are depicted in light grey. (G) Number of patients per participant in whom ctDNA was applied for clinical decision-making. The dashed red line indicates the median (12 patients), and the blue dashed line indicates the mean value (28 patients).

Kit (Macherey Nagel, Düren, Germany). Previously reported mutations from pathological tissue analysis for the respective cases were targeted using Oncobit PM Kits for *BRAF* V600E, V600D, and V600R. Analyses were performed by droplet digital PCR on a QX600 Droplet Reader (Bio-Rad, Feldkirchen, Germany). Results were reported qualitatively (detectable/non-detectable) and, where applicable, quantitatively as variant allele frequency (VAF) in percent.

2.4. Statistical analysis

Anonymous survey responses were collected via Excel and imported into Python (Google Colab) for analysis. Visualizations were created using Altair, matplotlib, and pywaffle (Python v3.10). Country-level data were standardized and enriched using the pycountry package. Pie charts and bar graphs were generated using GraphPad Prism (version 10.4.0). No inferential statistics were applied, as the primary aim was to describe and aggregate expert opinions.

3. Results

3.1. Participant characteristics and current use of ctDNA

A total of 116 melanoma experts completed the survey, representing 27 countries across Europe, North America, Asia, and Australia (Fig. 1A). The majority were medical oncologists (n = 62), followed by dermatologists specialized in dermatooncology (n = 41) (Fig. 1B). Approximately 44% of respondents reported having more than 20 years of experience in the field (Fig. 1B). For stage I and II melanoma, most participants reported involvement in up to ten patient cases per month. In contrast, for stage III-IV melanoma, most indicated involvement in more than ten cases monthly (Fig. 1C). In the adjuvant setting, participants were broadly involved in clinical decision-making, while in the neoadjuvant setting, most reported fewer than eleven cases per month. When asked about the current implementation status of ctDNA testing, 32 participants (27.6%) reported using ctDNA in both clinical practice and research, while the highest proportion indicated research use only (n = 40, 34.5%). Sixteen participants (13.8%) expressed a desire to establish ctDNA testing in their clinical practice, whereas eighteen (15.5%) had no such plans (Fig. 1D). At the time of the survey, 45% of respondents reported using ctDNA results to inform clinical decision-making, while 74% were actively involved in ctDNA-related research (Fig. 1E). Clinical ctDNA use was reported from the United States, Canada, Australia, and several European countries, while respondents from South America and parts of Asia indicated no current use (Fig. 1F). Among participants using ctDNA clinically, the number of patients for whom ctDNA-informed decisions were made varied widely, ranging from single cases to more than 300, with a median of twelve patients and a mean of 28 patients per participant (Fig. 1G).

3.2. Opinion on current clinical utility of ctDNA

After assessing participants' experience with ctDNA, the survey evaluated their opinions on its clinical applicability in the treatment of melanoma. Utility was rated on a scale from zero (not valuable) to five (very valuable). The lowest value was attributed to confirming melanoma diagnosis (mean 0.95) and to early-stage disease (AJCC-v8 stage I-IIA, mean 1.04 and 1.54; Fig. 2). In contrast, ctDNA was rated as most valuable in AJCC-v8 stage IV disease (mean 3.82), for MRD detection (mean 3.63), and for detecting recurrent disease (mean 3.85; Fig. 2). A heatmap analysis revealed no clear association between positive or negative ratings and participants' prior clinical use of ctDNA or involvement in ctDNA research (Supplementary Figure 1).

Consistent with these findings, ctDNA was considered a reliable tool for detecting relapse by 59% of respondents (Fig. 3A). Most participants agreed that ctDNA correlates well with clinical and radiographic response (80% yes vs. 4% no) (Fig. 3A). Integration of ctDNA into routine post-treatment surveillance was supported by 82% (Fig. 3A). To explore implementation preferences, participants were asked about panel size, testing type, and practical aspects such as costs and turn-around time (Fig. 3B). Interestingly, most participants did not favor broad mutation panels, which could be associated with expenses and delays. Instead, smaller, targeted next-generation sequencing (NGS) panels (32.8%) or predefined, i.e., tumor-agnostic approaches (31.9%) were preferred (Fig. 3B).

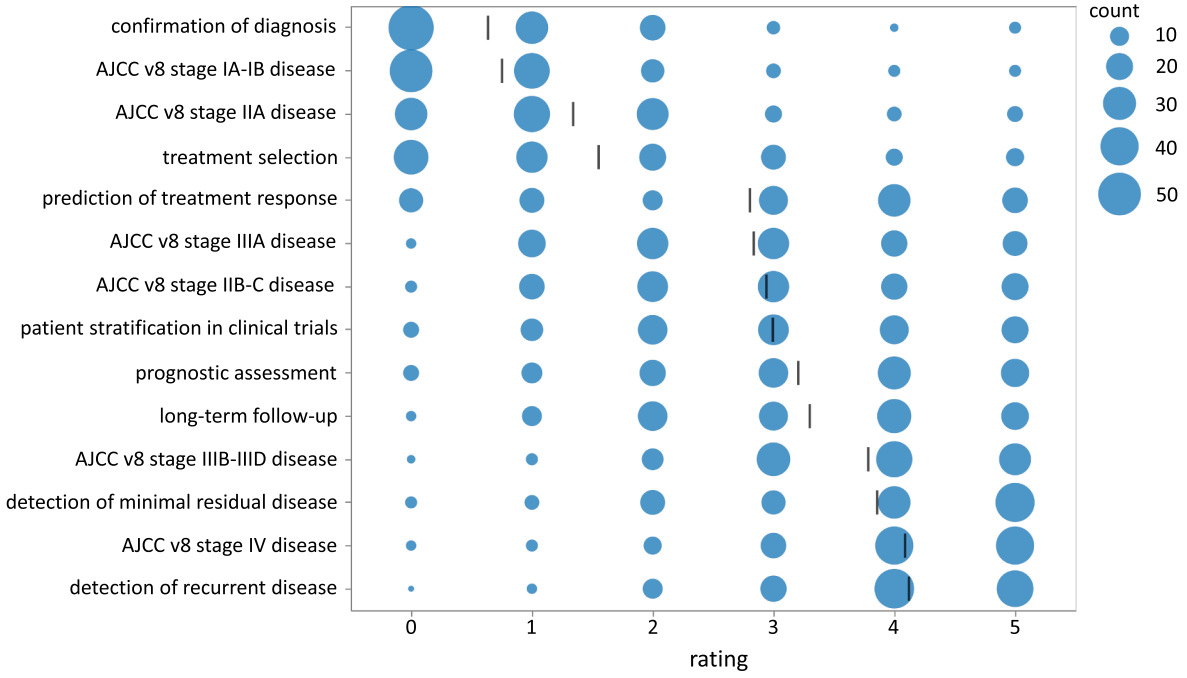

Fig. 2. Current utility of ctDNA in selected melanoma scenarios. Ratings of the clinical value of ctDNA in different scenarios on a scale from 0 (not valuable) to 5 (very valuable). The bubble size visualizes the number of participants selecting a given score. Vertical black lines represent the mean score for each scenario. The order of appearance of scenarios is based on an increasing mean score, displaying the highest score at the bottom of the plot.

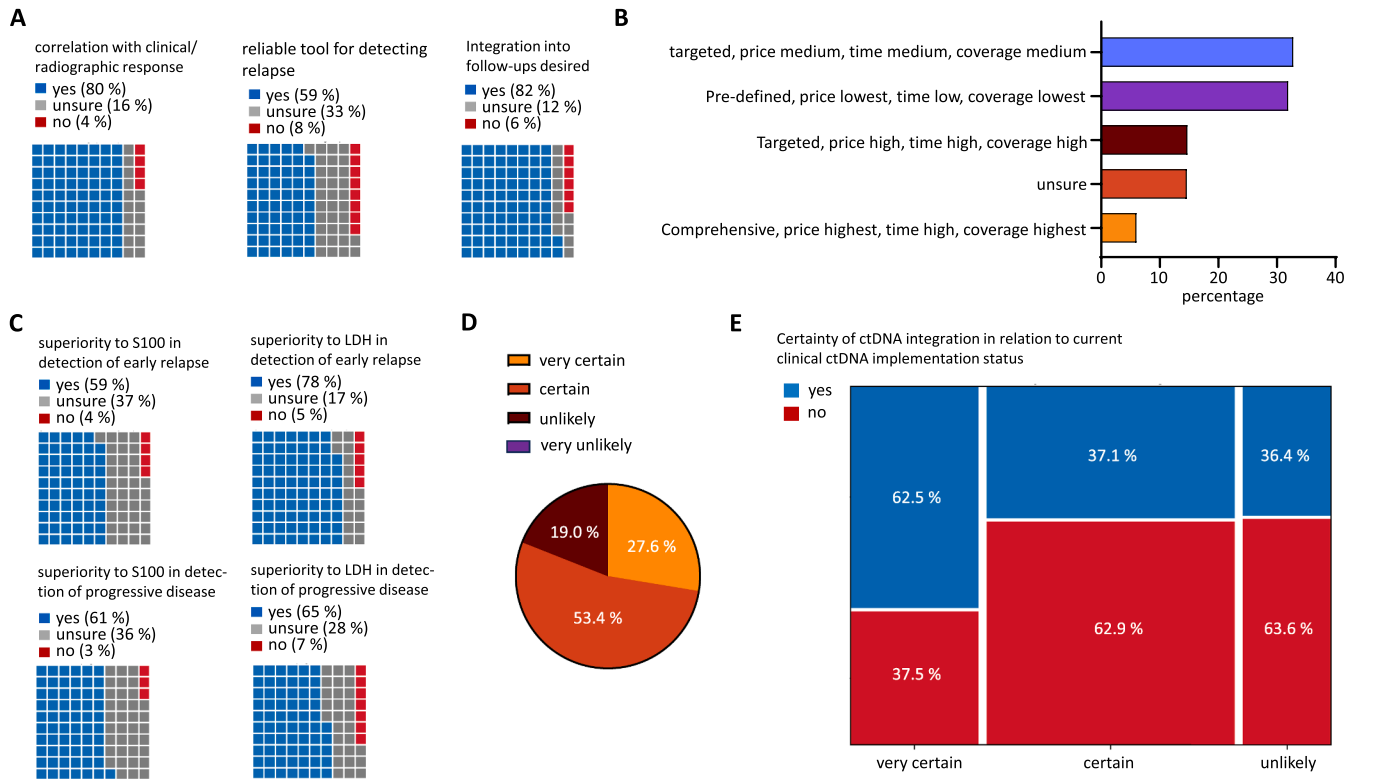

Fig. 3. Perceptions on clinical applicability, testing logistics, and implementation potential. (A) Waffle charts showing respondents' agreement on whether ctDNA correlates with clinical or radiographic response (left), to which ctDNA reliably detects a disease relapse (center), and to which ctDNA should be integrated into follow-ups. Answers are color-coded in blue (yes), grey (unsure), and red (no). (B) Preferences regarding ctDNA implementation strategies, illustrating favored panel size, time-to-results, coverage volume, price range, and location of analysis (on-site or externally). (C) Comparative value of ctDNA versus the serum markers S100 and lactate dehydrogenase (LDH) in detecting early relapse in adjuvant disease (top) and disease progression in unresectable stage IV disease (bottom). (D) Likelihood of ctDNA integration into routine clinical practice within the next five years. (E) Mosaic plot showing respondents' certainty about integrating ctDNA into routine clinical practice within the next five years, stratified by whether ctDNA is currently used clinically at their site (yes/no).

Next, ctDNA was compared to established melanoma markers S100 and LDH (Fig. 3C). In AJCC-v8 stage II/III disease without evidence of disease, ctDNA was considered superior to S100 (59%) and LDH (78%) for early relapse detection (Fig. 3C). In unresectable stage IV disease, ctDNA was rated superior to S100 (61%) and LDH (65%) for detecting progression (Fig. 3C). Finally, participants were asked about the likelihood of ctDNA being integrated into routine care within the next five years (Fig. 3D). None selected "very unlikely". The majority expected implementation to be "certain" (53.4%) or "very certain" (27.6%). Both participants with and without current clinical use of ctDNA selected these higher categories, although those already using ctDNA clinically more often indicated a higher level of certainty (Fig. 3E).

3.3. Current challenges

To identify barriers to clinical adoption, participants selected limiting factors from a predefined list. The results were visualized in an UpSet plot showing frequencies and combinations (Fig. 4). The most frequently cited barriers were reimbursement uncertainty (82%), lack of standardized guidelines (83%), and the need for large prospective trials (85%). Importantly, the responses selected combinations of barriers rather than single factors, underscoring that multiple issues are perceived as critical and must be addressed in parallel.

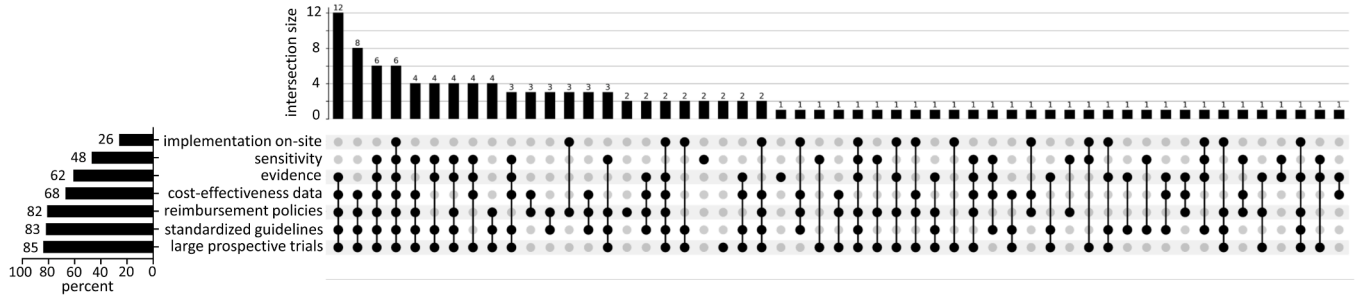

Fig. 4. Barriers to routine implementation of ctDNA testing in melanoma care. UpSet plot visualizing perceived barriers to routine clinical implementation of ctDNA. Multiple answers were allowed. Upper bar chart: Each bar indicates the number of participants reporting a specific combination of limiting factors, including lack of reimbursement, missing guidelines, insufficient evidence, and infrastructural or operational challenges. Lower panel: Black dots connected by lines illustrate the corresponding intersections of reported barriers per combination. Left bar chart: Percentage of participants who selected each barrier, highlighting the most frequently cited limitations.

3.4. Use of ctDNA in real-world and hypothetical scenarios

In addition to barriers, the survey assessed how ctDNA is used in real-world practice and how it might be applied under ideal conditions of approval and reimbursement. In the first vignette, which outlined a patient with rapidly progressing advanced melanoma (Supplementary Figure 2A-C), 82.8% of participants indicated that they would initiate BRAFi/MEKi therapy based on ctDNA if tissue analysis were pending (Fig. 5A). If tissue analysis was not feasible, this proportion increased to 93.9%. When asked about adjuvant treatment decisions between anti-PD-1 monotherapy and BRAFi/MEKi treatment, 37.1% would offer BRAFi/MEKi as an alternative option if tissue results were pending, and 56.8% if tissue analysis was not feasible (Fig. 5A). For relapse monitoring in the adjuvant setting, nearly 84% of participants supported the use of ctDNA in stage IV and IIIB-IIID disease (Fig. 5B). In stage IIIA, the proportion of ctDNA proponents was lower (60.3%), with a noticeable share of participants (20.7%) expressing uncertainty and 18.9% opting against its use (Figure 5B). For stages IIC and IIB, ctDNA remained the favored option, although a considerable proportion selected "unsure" or "no" (34.5% IIB, 24.3% IIC). In stage I and IIA disease, most respondents refrained from using ctDNA, citing limited perceived utility in early-stage settings. Notably, the share of “no” responses increased with decreasing stage, except for stage IIIA, which resembled stage IIB (17.2%; Fig. 5B).

The second vignette addressed MRD monitoring in patients with unresectable, advanced disease (Supplementary Figure 3A-C). Here, 80% supported the use of ctDNA for MRD assessment, and 78% considered it suitable to accompany routine diagnostics during follow-up (Fig. 5C). In the third vignette, ctDNA was presented as an adjunct to S100 and LDH in cases with unclear radiographic findings (Supplementary Figure 4A-D). Among patients without prior metastases, 77% regarded ctDNA as helpful, while 8% did not. In cases with known metastases, 68% supported ctDNA, and 15% would not use it (Fig. 5D). The fourth vignette addressed CNS metastases (Supplementary Figure 5A-B). Here, 62% did not see added value of ctDNA from blood, but 66% considered ctDNA from cerebrospinal fluid useful (Fig. 5E). The final vignette addressed the use of ctDNA in monitoring treatment response and the optimal timing for switching therapies (Supplementary Figure 6A-D). Most participants (74.1%) supported the use of ctDNA in this context, 17.2% were unsure, and 8.7% would not use it (Fig. 5F). Regarding testing frequency, 49.1% preferred monthly intervals, and 31.0% favored quarterly testing (Fig. 5G).

4. Discussion

This international expert survey provides a comprehensive assessment of current perceptions, applications, and barriers regarding the real-world clinical use of ctDNA in melanoma. Our findings corroborate prior research, suggesting that ctDNA is most valuable in advanced disease, particularly for detecting MRD (including the neoadjuvant setting) and guiding relapse surveillance [5,7]. Beyond serving as an early marker of relapse risk, ctDNA-based MRD assessment may help identify patients at high risk of imminent clinical progression, which could potentially enable earlier therapeutic intervention or adaptation. Emerging data also suggest that ctDNA dynamics and clearance could serve as an endpoint for treatment escalation or de-escalation in future ctDNA-guided management strategies [7]. In contrast, ctDNA was rated less valuable in stage I/IIA melanoma, which mirrors limited enthusiasm for its application in very low relapse-risk settings. This constraint likely stems from a shared perception that recurrence risk in early disease is

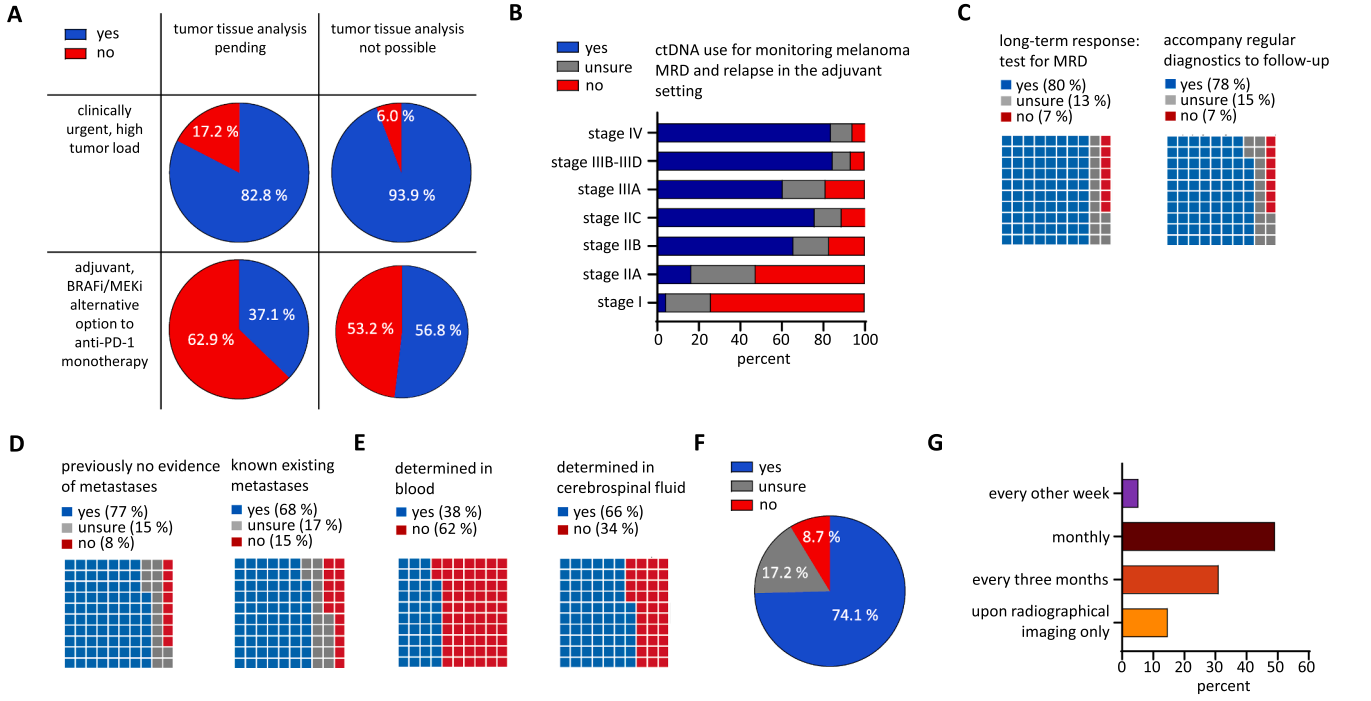

Fig. 5. Perspectives on the use of ctDNA in an “ideal” world of approval and reimbursement. (A) Proportion of participants who would initiate a targeted treatment with *BRAF*- and *MEK*-inhibitors based on ctDNA results if tumor tissue analysis was pending or not possible, whilst at the same time the patient would exhibit an urgent medical need with high tumor load or in an adjuvant setting. (B) Stage-specific use of ctDNA to follow up on melanoma minimal residual disease (MRD) and relapse detection, assuming the patient would be a candidate for adjuvant therapy. (C-E) Waffle chart depicting the opinion on ctDNA accompanying (C) regular diagnostics to test for MRD or regular diagnostics to follow-up on disease status, (D) in radiographically ambiguous cases with and without prior evidence of metastases, and (E) for central nervous system (CNS) metastases using blood or cerebrospinal fluid as a basis for ctDNA determination. Answers are color-coded with blue (yes), grey (unsure), and red (no). (F) Proportion of participants who would integrate ctDNA in clinical decision-making upon monitoring of treatment responses. Answers are color-coded in blue (yes), grey (unsure), and red (no). (G) Percentage of participants voting for a respective frequency at which ctDNA should be determined when established in routine diagnostics.

low and can often be addressed by tissue-based analyses [13]. However, it could also reflect the repeated perception that current ctDNA technologies fail to detect low-level ctDNA in a proportion of patients who are nevertheless destined to recur. The survey also highlighted uncertainty regarding the role of ctDNA in CNS disease: Most participants did not support blood-based monitoring in this context, consistent with the known limitations of peripheral assays for detecting intracranial disease [14]. Nonetheless, a substantial proportion favored ctDNA analysis in cerebrospinal fluid, which could indicate interest in compartment-specific liquid biopsies that may overcome the blood-brain barrier.

Notably, in urgent clinical situations characterized by a high tumor burden and limited time for tissue genotyping, many participants expressed a willingness to base therapeutic decisions solely on ctDNA. A considerable proportion reported they would initiate BRAF/MEK-directed therapy solely on ctDNA results when tissue analysis was pending or not feasible. This finding underscores the growing confidence in the clinical validity of ctDNA as a time-sensitive decision-making tool, an aspect that has been less emphasized in previous studies [15,16].

Overall, ctDNA was considered a valuable complement to older biomarkers such as S100 and LDH, especially in cases with diagnostic ambiguity. This aligns with earlier reports showing that ctDNA can outperform conventional markers in detecting subclinical progression and refining assessments in advanced disease [4,17]. Furthermore, it has been associated with high levels of acceptability by patients who view it as "more scientific" than other standard tests [11]. Despite this confidence, routine implementation remains constrained by systemic barriers: participants most frequently cited the need for prospective studies evaluating the clinical benefit of ctDNA monitoring, standardized guidelines, and clear reimbursement policies, whilst logistical and infrastructure issues were less prominent. This suggests that the implementation gap is primarily due to a lack of data showing improved clinical outcomes, regulatory, and financial, rather than technical issues [2,18].

Accordingly, there is a pressing need to generate high-level clinical evidence and establish standardized testing frameworks. Initial studies, such as COMBI-AD, CAcTUS, DyNAMIc, and Detection-2, have begun to define the prognostic and predictive value of ctDNA in selected scenarios [7,19–21]. However, large, prospective, multi-center trials across all disease stages and treatment contexts remain essential to define actionable thresholds and optimal sampling strategies.

From a guideline perspective, the clinical relevance of ctDNA in melanoma is increasingly acknowledged. The 2024 EADO guidelines provide a structured overview of liquid biopsy modalities and highlight ctDNA as the most extensively studied marker [22]. Specific applications, such as MRD detection, longitudinal monitoring, and early resistance, are discussed, and key studies, including translational analyses from major trials, are cited to support its potential clinical utility. While these recommendations reflect growing scientific support, they stop short of issuing operational guidance for routine clinical use. Specific indications, testing intervals, performance thresholds, or decision-making algorithms are not yet defined. The 2025 ESMO melanoma guideline already permits the use of ctDNA for *BRAF V600* mutation testing when tumor tissue is unavailable, which represents an acknowledged clinical application [23]. While both documents recognize the clinical relevance of ctDNA, they do not yet provide stage-specific or scenario-based recommendations for its broader integration into melanoma care. Building on current prospective trials and emerging real-world data, future guideline iterations will be essential to define the role of ctDNA across additional decision points, including treatment monitoring, surveillance, and risk-adapted management strategies.

In parallel with clinical guidance, the survey also explored practical aspects of ctDNA testing, revealing clear preferences among experts for streamlined, pragmatic approaches to implementation. Experts favored streamlined testing strategies with small to mid-size targeted panels and short turnaround times. This preference reflects a shift toward pragmatic, clinically actionable efficiency, where assays optimized for cost, speed, and feasibility are prioritized over broad genomic profiling. Importantly, such streamlined approaches also align positively with reimbursement considerations, as they reduce overall testing costs while still delivering clinically relevant information. This suggests that smaller, efficient panels may not only be more acceptable to clinicians but also more feasible to integrate within healthcare systems facing reimbursement constraints. Successful clinical integration of ctDNA will therefore depend not only on analytical performance, but also on alignment with real-world oncology workflows. In other solid tumors, such as colorectal cancer, ctDNA-based surveillance is supported by large prospective clinical studies, whereas in melanoma, prospective evidence informing actionable thresholds, standardized testing intervals, and clinical decision-making frameworks remains less well established [24].

This study has limitations inherent to expert opinion surveys, including subjective assessments influenced by individual experience and institutional capacities. Furthermore, the cohort primarily consisted of experts from academic melanoma centers, which may limit its generalizability. In addition, survey participation was voluntary, raising the possibility of self-selection bias toward those particularly engaged in ctDNA research. Moreover, 38.7% of invited members completed the survey. As participation was anonymous, characteristics of non-responders (e.g., profession, geographical location, or level of clinical exposure to ctDNA) could not be analyzed. It is therefore possible that specific professional groups or regions were underrepresented among respondents, which may influence the overall perception of ctDNA utility and implementation readiness reflected in the results. The survey relied on hypothetical vignettes, which, although derived from real patient cases, cannot fully capture the complexity and heterogeneity of clinical practice. Regional representation was uneven, with limited responses from South America, Africa, and parts of Asia, which may influence the global perspective. Clinical practice environments and healthcare system structures differ internationally, and perspectives from non-academic settings may add important insights regarding implementation pathways. Future surveys and prospective studies should therefore aim to incorporate a broader range of geographical regions and practice settings to enhance global applicability. Finally, the findings reflect opinions at a specific time point and may evolve rapidly as new evidence, guidelines, or reimbursement policies emerge. Despite inherent limitations, the breadth of international participation strengthens the relevance of these findings and underscores the global momentum toward incorporating ctDNA into melanoma care. Strengthening international collaborative networks and facilitating broad participation in prospective multicenter trials will be important to ensure that evidence generation and implementation strategies for ctDNA are applicable across diverse healthcare systems.

5. Conclusions

This international survey draws on insights from key opinion leaders across 27 countries and provides the most comprehensive assessment to date of expert opinions on the clinical use of ctDNA in melanoma. It highlights areas of consensus, such as MRD detection, relapse surveillance, and urgent decision-making when tissue genotyping is delayed or impossible. Also, it identifies limitations in early-stage disease and CNS involvement. This work outlines both the perceived potential and the barriers and thereby defines actionable priorities for the field, including prospective validation, guideline development, and reimbursement strategies. Addressing these priorities will be essential to support the broader clinical integration of ctDNA into routine melanoma care.

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Ethics statement

This study was conducted and constent was obtained in accordance with the Declaration of Helsinki and approved by the Ethics Committee of the Hamburger Ärztekammer (PV5392–3704-BO-ff, 2025-101477-BO-ff).

Declaration

The author Alexander Eggermont is the Editor-in-Chief of the EJC and was not involved in the editorial review or the decision to publish this article. The author Jessica Hassel is an Editor of the EJC and was not involved in the editorial review or the decision to publish this article.

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with Philogen that includes: consulting or advisory and funding grants. Jonathan S Zager reports a relationship with Delcath Systems Inc that includes: consulting or advisory and funding grants. Jonathan S Zager reports a relationship with Replimune that includes: consulting or advisory. Axel Hauschild reports a relationship with Merck Sharp & Dohme UK Ltd that includes: consulting or advisory, funding grants, and speaking and lecture fees. Axel Hauschild reports a relationship with Merck that includes: consulting or advisory, funding grants, and speaking and lecture fees. Axel Hauschild reports a relationship with Philogen that includes: consulting or advisory, funding grants, and speaking and lecture fees. Axel Hauschild reports a relationship with Pierre Fabre that includes: consulting or advisory, funding grants, and speaking and lecture fees. Axel Hauschild reports a relationship with Regeneron Pharmaceuticals Inc that includes: consulting or advisory, funding grants, and speaking and lecture fees. Axel Hauschild reports a relationship with Roche that includes: consulting or advisory, funding grants, and speaking and lecture fees. Axel Hauschild reports a relationship with Sanofi Genzyme that includes: consulting or advisory, funding grants, and speaking and lecture fees. Axel Hauschild reports a relationship with Novartis that includes: consulting or advisory, funding grants, and speaking and lecture fees. Axel Hauschild reports a relationship with Eisai that includes: consulting or advisory, funding grants, and speaking and lecture fees. Axel Hauschild reports a relationship with Immunocore that includes: consulting or advisory. Axel Hauschild reports a relationship with Replimune that includes: consulting or advisory. Axel Hauschild reports a relationship with Seagen that includes: consulting or advisory. Christoffer Gebhardt reports a relationship with Bristol Myers Squibb Co that includes: consulting or advisory, speaking and lecture fees, and travel reimbursement. Christoffer Gebhardt reports a relationship with GSK that includes: speaking and lecture fees. Christoffer Gebhardt reports a relationship with Immunocore that includes: consulting or advisory and speaking and lecture fees. Christoffer Gebhardt reports a relationship with Merck Sharp & Dohme UK Ltd that includes: consulting or advisory and speaking and lecture fees. Christoffer Gebhardt reports a relationship with Novartis that includes: consulting or advisory and speaking and lecture fees. Christoffer Gebhardt reports a relationship with Pierre Fabre that includes: consulting or advisory, speaking and lecture fees, and travel reimbursement. Christoffer Gebhardt reports a relationship with Sanofi that includes: consulting or advisory and speaking and lecture fees. Christoffer Gebhardt reports a relationship with Sun Pharmaceutical Industries Ltd that includes: consulting or advisory, speaking and lecture fees, and travel reimbursement. Christoffer Gebhardt reports a relationship with Sysmex that includes: consulting or advisory and speaking and lecture fees. Christoffer Gebhardt reports a relationship with Dermatologic Cooperative Oncology Group (DeCOG) that includes: board membership. Christoffer Gebhardt reports a relationship with Hiege Stiftung that includes: board membership. Christoffer Gebhardt reports a relationship with Erich und Gertrud Roggenbuck Foundation for Cancer Research that includes: board membership. Christoffer Gebhardt reports a relationship with Dermagnostix that includes: equity or stocks. Christoffer Gebhardt reports a relationship with Dermagnostix R&D that includes: equity or stocks. Teresa Amaral has patent #18/386 licensed to Teresa Amaral. Teresa Amaral has patent #708 licensed to Teresa Amaral. Given his role as associate editor of the section melanoma and oncoimmunology of Annals of Oncology, Paolo Ascierto had no involvement in the peer review of this article and had no access to information regarding its peer review. Full responsibility for the editorial process for this article was delegated to another EJC journal editor. Nathan Fekade, Katharina Raabe, Daniel J Smit, Laura Adam, Alessandra Ruenger, Paul Lorigan, Alberto Wainstein, Helen Rizos, and Klaus Pantel have nothing to declare.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.ejca.2026.116676.

Data availability statement

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

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