MDForLives

THE GLOBAL PULSE OF HEALTHCARE · ONCOLOGY & HEMATOLOGY INSIGHT REPORT

Overall Survival in Oncology: When Should Surrogate Endpoints Count?

Responses from oncology and hematology clinicians on overall survival, surrogate endpoints, molecular response, patient-reported outcomes, treatment toxicity, payer barriers, and accelerated approval: where OS remains indispensable, where earlier endpoints are gaining credibility, and what evidence clinicians still need before they act.

Context → Signal → Judgement → Action

72	**6**	**70.8%**	**8945208**
Survey records	Countries represented USA · UK · Canada · Italy · France · Germany	Completion rate	Survey ID

WHY THIS REPORT

Oncology increasingly has to decide whether waiting for OS clarifies benefit or delays it.

Overall survival is easy to understand and difficult to argue with: patients live longer or they do not. Yet modern oncology creates situations where the endpoint can take years to mature, be diluted by treatment crossover, be influenced by several effective post-progression therapies, or arrive after an earlier outcome has already changed clinical practice. The tension is especially visible in early-stage disease, long-survival hematologic malignancies, biomarker-defined populations, and settings where durable disease control or organ preservation may matter long before mortality separates.

The MDForLives survey asks clinicians to make those trade-offs directly. It examines when OS should remain the primary approval benchmark, how a modest survival gain changes prescribing when chronic toxicity rises, where MRD or ctDNA may be mature enough to support earlier approval, whether persistent molecular negativity is actionable enough to reduce therapy, how much weight PRO/QoL should carry, what drives late-line shared decisions, how clinicians interpret PFS/EFS gains without an OS benefit, where payers create friction, and what would make accelerated approval more trustworthy.

The pattern is not an anti-OS story. It is a contextual evidence story. Respondents keep OS central in many settings, but they also accept surrogate endpoints when the disease context, magnitude of benefit, patient priorities, and follow-up evidence make the earlier signal clinically usable. The biggest uncertainties appear at the transition points: when an endpoint moves from prognostic signal to approval basis, from trial result to prescribing decision, and from regulatory access to payer access.

> **Survey lens.** MDForLives survey SGID 8945208 captured 72 survey records, 51 complete responses, and a 70.8% completion rate across 6 countries: USA, UK, Canada, Italy, France, and Germany. Q4–Q14 include 52 responses because one partial respondent answered through these clinical questions; Q15–Q16 include 51 responses. The open-ended Q18 contains 20 visible responses, including a small number of non-specific answers. Internal operational, validation, required-text, after-survey, and honeypot fields are excluded from analysis.

CLINICAL AND REGULATORY CONTEXT

The endpoint framework is broadening, but OS is still the reference point clinicians have to reconcile.

NCI continues to place overall survival at the top of its hierarchy of treatment-study endpoints because it is direct, patient-important, and comparatively resistant to interpretation bias. At the same time, FDA's Oncology Center of Excellence is actively working on a wider endpoint framework. Project Endpoint describes early and late endpoints as complementary. FDA's August 2025 draft guidance on OS focuses on how survival should be assessed in randomized oncology trials even when OS is not the primary endpoint, including its role as a pre-specified safety endpoint.

Molecular and patient-centered endpoints are also moving forward in specific contexts. FDA issued final guidance in 2024 on ctDNA in early-stage solid-tumor drug development and on core patient-reported outcomes in cancer clinical trials. Its longstanding MRD guidance covers hematologic malignancies, and a January 2026 draft guidance specifically addresses MRD and complete response as primary endpoints to support accelerated approval in multiple myeloma. Project Confirm, meanwhile, emphasizes that accelerated approval based on a surrogate endpoint is paired with confirmatory evidence intended to verify clinical benefit. The survey sits directly inside this evolving evidence architecture.

External clinical and regulatory context is provided for interpretation. MDForLives survey findings remain the source for all respondent percentages in this report.

EXECUTIVE SUMMARY

Six findings that show why endpoint choice is becoming a clinical judgement, not only a trial-design decision.

INSIGHT 01

OS becomes setting-specific

40.4% Keep OS for late-stage or relapsed disease while allowing surrogate endpoints to replace it in selected early or adjuvant settings.

INSIGHT 02

Toxicity changes the meaning of modest OS gain

59.6% Would offer a higher-toxicity regimen with a modest OS benefit mainly to younger, fit patients who prioritize maximum survival.

INSIGHT 03

MRD readiness is strongest in hematologic disease

46.2% Choose hematologic malignancies as the setting most ready for negative MRD/ctDNA to support standalone approval.

INSIGHT 04

Late-line decisions can prioritize lived benefit

40.4% Say symptom palliation, preserved function, and daily QoL most often drive the final shared decision.

INSIGHT 05

PFS/EFS is accepted with an explicit caveat

55.8% Would prescribe a robust PFS/EFS-improving drug without OS benefit while explaining that total lifespan is not yet confirmed.

INSIGHT 06

RWE is the preferred post-approval confidence lever

43.1% Want mandatory real-world evidence tracking alongside confirmatory trials for accelerated approvals.

01

OVERALL SURVIVAL BENCHMARK

OS remains the anchor, but most respondents do not want one endpoint rule for every setting

40.4% say OS is necessary in late-stage or relapsed settings, while surrogate endpoints should replace it in selected early, adjuvant, or other settings.

CONTEXT

OS is the most direct trial endpoint because it answers whether patients live longer. The challenge is timing and interpretability. In cancers with long natural histories, multiple effective subsequent therapies, or substantial crossover, an OS difference may take years to emerge or may be diluted by what happens after progression. That creates a familiar oncology tension: the most definitive endpoint can also be the slowest or most confounded endpoint.

WHAT THE DATA SHOWS

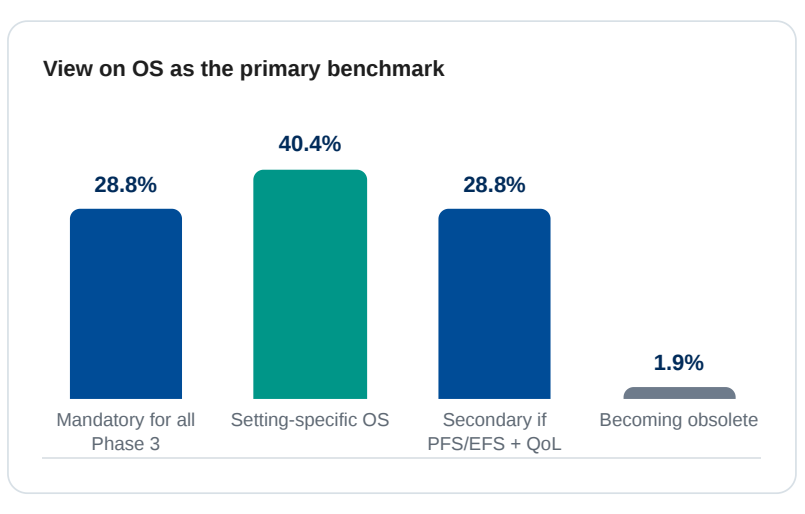
Among 52 respondents, 21 clinicians (40.4%) choose a setting-specific position: OS should remain necessary in late-stage or relapsed disease, while surrogate endpoints can replace it in early-stage, adjuvant, or selected contexts. Fifteen (28.8%) would keep OS mandatory for all definitive Phase 3 approvals. Another 15 (28.8%) would downgrade OS to a secondary endpoint when significant PFS/EFS and quality-of-life benefits are shown. Only one respondent (1.9%) says OS is becoming obsolete.

THE INSIGHT

The center of gravity is not rejection of OS. It is conditional use. Two equally sized groups sit on either side of the largest setting-specific group, showing a profession negotiating where the evidentiary threshold should change rather than whether survival matters at all. The survey suggests that endpoint appropriateness is becoming inseparable from treatment intent, expected survival, and the likelihood that subsequent therapy will blur the OS signal.

WHY IT MATTERS

For clinicians reading a positive trial, the practical question becomes "What clinical uncertainty does this endpoint actually resolve?" A PFS or EFS gain may be highly meaningful in a curative-intent or long-survival setting, but a late-stage regimen with substantial toxicity may still need mature OS to show that the trade-off improves the outcome patients value most. FDA's Project Endpoint and 2025 draft OS guidance reflect the same need to consider early and late endpoints together rather than in isolation.


View on OS as the primary benchmark

02

MODEST OS BENEFIT VS TOXICITY

A modest OS gain becomes a patient-selection decision when chronic toxicity rises

59.6% would offer the regimen primarily to younger, fit patients who prioritize maximum survival over side-effect profiles.

CONTEXT

A hazard ratio or median survival extension does not carry toxicity, frailty, daily function, immune adverse events, infusion burden, or financial exposure inside the number. Oncologists have to translate an average trial benefit into a patient-specific benefit-risk decision, especially when the OS extension is modest and the regimen adds persistent Grade 2/3 toxicity or complex immune or hematologic adverse events.

WHAT THE DATA SHOWS

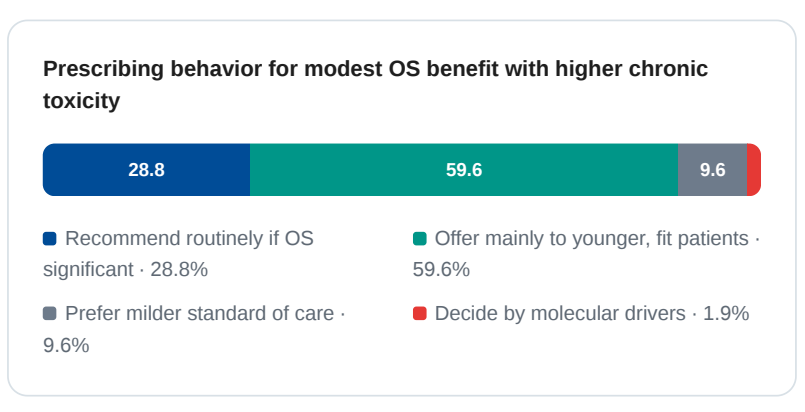
Thirty-one of 52 respondents (59.6%) say their primary behavior is to offer the higher-toxicity regimen mainly to younger, fit patients, typically ECOG 0–1, who prioritize maximum survival. Fifteen (28.8%) would routinely recommend any statistically significant OS extension when toxicity is manageable. Five (9.6%) generally prefer the milder standard of care to preserve daily QoL unless the patient explicitly requests the more aggressive option. One respondent (1.9%) says the decision is driven strictly by genomic or molecular markers rather than population OS averages.

THE INSIGHT

The dominant response converts a population-level endpoint into a selection framework. Most clinicians are not treating the modest OS benefit as a universal prescription signal. They are asking who is fit enough, motivated enough, and likely enough to experience the gain without losing too much function or quality of life. The smaller "routine recommendation" group shows that statistical significance still carries weight, but it is not the modal response.

WHY IT MATTERS

This matters because endpoint debates can become abstract if toxicity is separated from efficacy. A trial can meet OS and still leave a difficult bedside trade-off. For an older or frail patient, chronic toxicity may consume much of the extra time gained; for a younger, fit patient, the same trade-off may be acceptable. The clinical meaning of OS therefore depends on the treatment burden attached to it and the patient's own preference for longevity versus function.


Prescribing behavior for modest OS benefit with higher chronic toxicity

03

MRD / CTDNA AS APPROVAL ENDPOINTS

Molecular response is closest to standalone-endpoint status in hematologic malignancies

46.2% identify hematologic malignancies as the setting most ready for negative MRD/ctDNA to support approval without waiting for OS.

CONTEXT

MRD and ctDNA can reveal disease persistence or clearance far earlier than radiographic progression or death. The appeal is obvious: an earlier molecular signal could shorten trials and move effective therapy to patients sooner. The risk is equally important: a biomarker can be prognostic without being a validated surrogate for how patients feel, function, or survive, and assay performance can vary across diseases and platforms.

WHAT THE DATA SHOWS

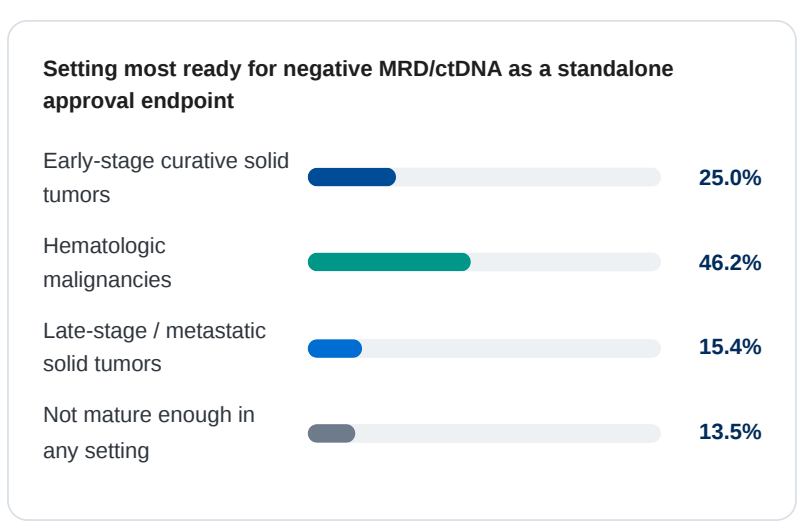
Twenty-four of 52 clinicians (46.2%) choose hematologic malignancies such as multiple myeloma, leukemia, and lymphoma as the most approval-ready setting. Thirteen (25.0%) choose early-stage curative solid tumors, including neoadjuvant or adjuvant settings. Eight (15.4%) choose late-stage or metastatic solid tumors to confirm complete molecular response. Seven (13.5%) say MRD is not yet mature enough to serve as a standalone approval endpoint in any setting.

THE INSIGHT

Respondent confidence follows endpoint maturity rather than a technology-first enthusiasm for liquid biopsy. Hematology leads by a clear margin, which is consistent with the longer regulatory experience of MRD in blood cancers. Early-stage solid tumors are the next strongest setting, where recurrence can take years and ctDNA may potentially provide an earlier window into residual disease. Metastatic solid tumors attract less confidence, where molecular clearance may be harder to interpret as a substitute for durable clinical benefit.

WHY IT MATTERS

FDA's 2020 final MRD guidance addresses hematologic malignancies, and its January 2026 draft guidance specifically discusses MRD and complete response as primary endpoints for accelerated approval in multiple myeloma. FDA's 2024 final ctDNA guidance for early-stage solid tumors also underscores assay standardization and methodological rigor. For oncologists, the practical takeaway is that "MRD negative" is not one universal evidence category; disease, assay, timing, and validation determine how far the signal can be trusted.


Setting most ready for negative MRD/ctDNA as a standalone approval endpoint

04

MRD-GUIDED DE-ESCALATION

Persistent MRD negativity changes treatment intensity before it changes the decision to stop

46.2% are moderately comfortable reducing dose or maintenance frequency after persistent MRD negativity, but would not stop therapy entirely.

CONTEXT

If molecular response is clinically meaningful, the next question is whether it can safely reduce treatment burden. That is a different evidentiary threshold from using MRD as a trial endpoint. Stopping therapy early carries asymmetric risk: a false sense of cure or insufficiently validated de-escalation could lead to relapse, while continuing treatment can add toxicity, long-term adverse effects, cost, and patient burden.

WHAT THE DATA SHOWS

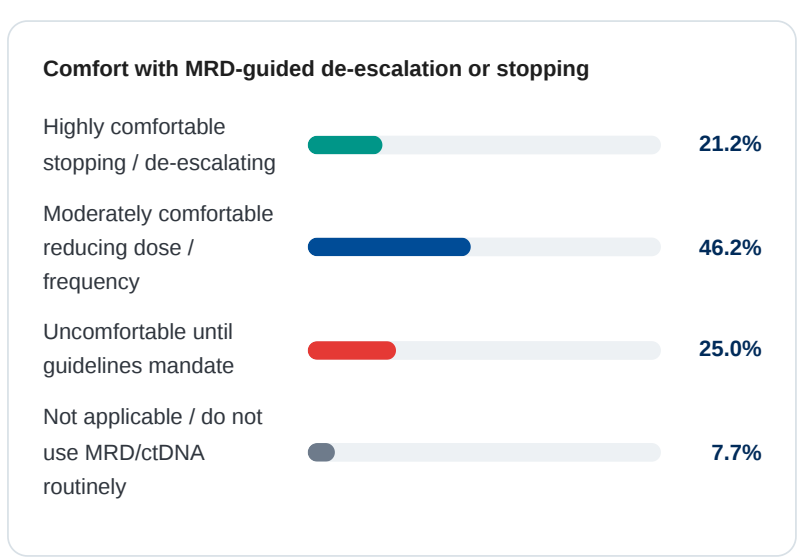
Twenty-four of 52 respondents (46.2%) take a middle position. They would reduce dose or maintenance frequency after confirmed, persistent MRD negativity but would not stop therapy entirely. Eleven (21.2%) are highly comfortable stopping or de-escalating based on persistent MRD negativity within clinical practice or protocol-driven trials. Thirteen (25.0%) are uncomfortable and prefer the full standard duration until guidelines explicitly mandate otherwise. Four (7.7%) do not currently use MRD/ctDNA testing in their routine workflow.

THE INSIGHT

The molecular signal appears more actionable for intensity adjustment than for complete cessation. That is a clinically important distinction. Respondents are willing to let MRD influence the pathway, but most stop short of treating a negative test as equivalent to proven cure. The largest group uses MRD as a reason to reduce exposure rather than eliminate therapy, which suggests that de-escalation may be the first major real-world use case before full treatment cessation becomes routine.

WHY IT MATTERS

For trial designers, this points toward studies that test MRD-guided treatment duration rather than assuming biomarker negativity automatically supports stopping. For clinicians, it reinforces the need to separate prognostic information from treatment-direction evidence. A negative molecular test can be reassuring and still require protocol support, disease-specific validation, and a clear monitoring strategy before it changes a standard duration of therapy.


Comfort with MRD-guided de-escalation or stopping

05

PRO / QUALITY OF LIFE

Patient-reported benefit has real weight, but most clinicians still pair it with an efficacy signal

50.0% would give validated PRO/QoL improvements secondary regulatory weight only when accompanied by statistically significant PFS/EFS gains.

CONTEXT

Patient-reported outcomes capture symptoms, functional status, treatment burden, and health-related quality of life in a way imaging and survival curves cannot. In oncology, their value is obvious when therapies have similar efficacy but very different day-to-day consequences. The harder question is whether a strong PRO/QoL improvement can compensate for neutral or non-significant OS in regulatory or HTA decisions.

WHAT THE DATA SHOWS

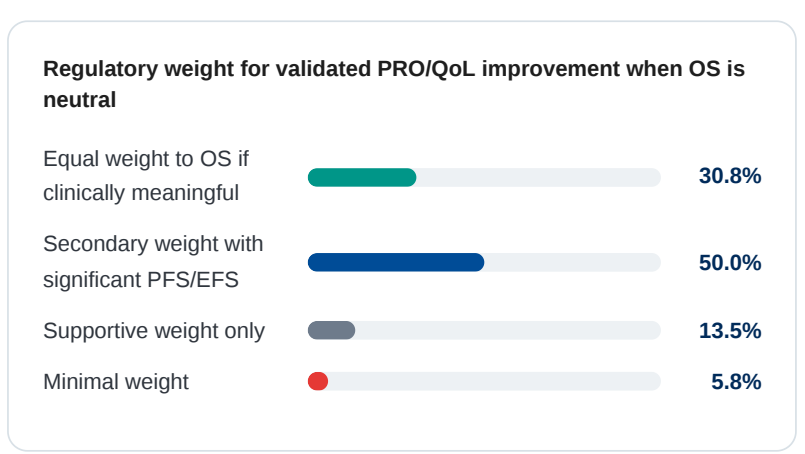
Twenty-six of 52 respondents (50.0%) assign PRO/QoL a secondary role that should support approval only when statistically significant PFS/EFS gains are also present. Sixteen (30.8%) would give clinically meaningful QoL improvement equal weight to OS if disease stabilization justifies full approval. Seven (13.5%) see QoL as supportive evidence for labeling and counseling but not a primary approval or reimbursement driver. Three (5.8%) give it minimal weight because they view subjective measures as too susceptible to bias.

THE INSIGHT

The largest group does not dismiss QoL; it embeds it inside a broader efficacy package. That differs from the bedside pattern later in the survey, where symptom palliation and preserved function become the largest single shared-decision driver. The divergence makes sense. Regulators need a reproducible population-level claim; clinicians and patients need to decide whether a treatment helps this person live in a way they value.

WHY IT MATTERS

FDA's 2024 final guidance on core PROs in cancer trials reflects the growing importance of systematic patient-reported evidence. The survey suggests that better PRO methodology could increase its influence, but most respondents are not ready to let QoL routinely replace conventional efficacy endpoints. The opportunity is therefore integration: survival, disease control, toxicity, and patient-reported function should be interpreted together when they answer different dimensions of benefit.


Regulatory weight for validated PRO/QoL improvement when OS is neutral

06

LATE-LINE SHARED DECISIONS

In advanced disease, the endpoint that wins the trial may not be the outcome that wins the decision

40.4% say symptom palliation, preserved function, performance status, and daily QoL most often drive the final late-line shared decision.

CONTEXT

Late-line care compresses multiple goals into one conversation. Patients may want more time, less disease progression, relief of symptoms, preserved independence, fewer hospital visits, lower toxicity, or simply a treatment that remains compatible with daily life. The endpoint used in a pivotal trial provides evidence, but the final choice often depends on which benefit matters most at that point in the illness trajectory.

WHAT THE DATA SHOWS

Twenty-one of 52 respondents (40.4%) choose symptom palliation, preservation of functional performance status, and daily QoL as the factor that typically drives the final shared decision. Seventeen (32.7%) choose expected OS extension, and 13 (25.0%) choose expected PFS/EFS from clinical trial data. Only one respondent (1.9%) selects treatment manageability, including schedule, route, toxicity, and financial burden, as the single dominant factor.

THE INSIGHT

The largest response category is patient-centered function rather than a survival statistic. That does not mean oncologists ignore OS. It means the endpoint hierarchy changes when the decision is no longer "Does this drug work in a trial?" but "What should this patient do now?" The difference between Q11 and Q12 is especially instructive: QoL is mostly supportive or secondary in regulatory evaluation, yet it becomes the largest single driver in late-line shared decision-making.

WHY IT MATTERS

Clinical-trial design and clinical decision-making solve different problems. Trials need standardized endpoints; shared decisions need preference-sensitive outcomes. Presenting OS, PFS/EFS, symptom benefit, functional burden, and toxicity as parallel pieces of evidence may therefore be more useful than forcing one endpoint to carry the entire definition of benefit at every stage of cancer care.

Factor that typically drives the final late-line shared decision

40.4% Symptom palliation, function, performance status, daily QoL

32.7% Expected OS extension

25.0% Expected PFS/EFS

1.9% Treatment manageability and financial toxicity

07

PFS / EFS WITHOUT OS

Most clinicians will use a strong PFS/EFS result without OS, but they keep the survival uncertainty explicit

55.8% call a robust PFS/EFS extension without OS benefit moderately acceptable and would prescribe while explaining that longer total lifespan is unconfirmed.

CONTEXT

A positive PFS or EFS result can be clinically valuable even when final OS is neutral, particularly if progression itself causes symptoms, organ damage, hospitalization, or loss of future options. But PFS and EFS are not identical to survival. The core communication problem is how to use a meaningful earlier benefit without implying a mortality benefit that the trial did not demonstrate.

WHAT THE DATA SHOWS

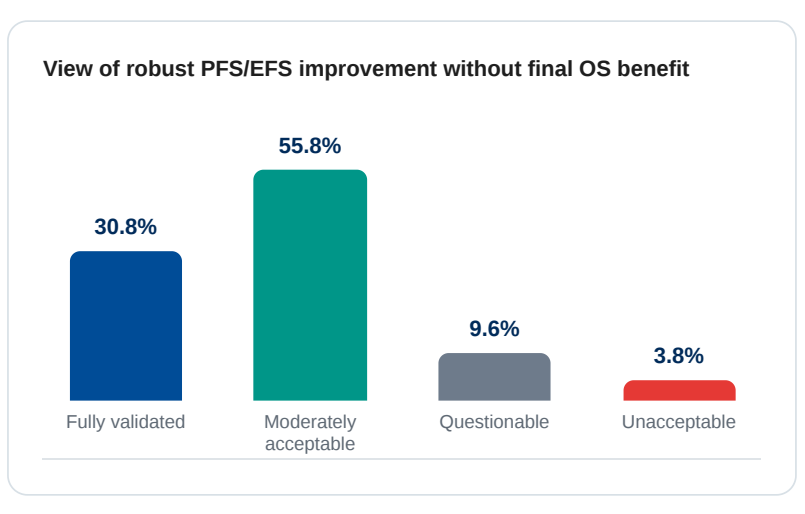
Twenty-nine of 52 respondents (55.8%) choose the middle position: prescribe the approved drug but inform the patient that it extends time without progression rather than confirmed total lifespan. Sixteen (30.8%) consider the PFS/EFS improvement fully validated because delaying progression can prevent organ damage, complications, or symptomatic relapse. Five (9.6%) regard the drug as questionable and would restrict use to patients who have exhausted alternatives with proven OS benefit. Two (3.8%) call it unacceptable, interpreting the missing OS effect as a warning about post-progression toxicity, ineffective subsequent lines, or trial-design limitations.

THE INSIGHT

The survey separates "clinically meaningful" from "equivalent to OS." Most clinicians are willing to act on robust disease-control evidence, but the dominant position is transparent conditional acceptance rather than full equivalence. This is a sophisticated evidence stance: PFS/EFS can justify action, while the absence of OS still changes how the benefit is described to the patient and how long-term confidence is framed.

WHY IT MATTERS

This matters for consent, guideline interpretation, and value assessment. A six-month PFS gain can be highly meaningful if it delays painful progression or preserves organ function, but it should not be translated automatically into six months of additional life. Clear endpoint language protects shared decision-making from turning a surrogate benefit into a stronger claim than the data support.


View of robust PFS/EFS improvement without final OS benefit

08

ACCESS AND POST-APPROVAL CONFIDENCE

Surrogate-based approvals can clear the regulator and still hit a payer barrier

42.3% say reimbursement or prior-authorization hurdles occasionally block prescribing of therapies approved on surrogate endpoints; 26.9% say this happens frequently.

CONTEXT

Accelerated approval is designed to move promising therapy to patients before definitive clinical benefit is fully mature. That regulatory speed does not guarantee immediate payer confidence. When an approval rests on response, PFS, EFS, pCR, or another surrogate, insurers and PBMs may ask whether the evidence is mature enough to justify coverage, especially when treatment cost is high or confirmatory trials are still ongoing.

WHAT THE DATA SHOWS

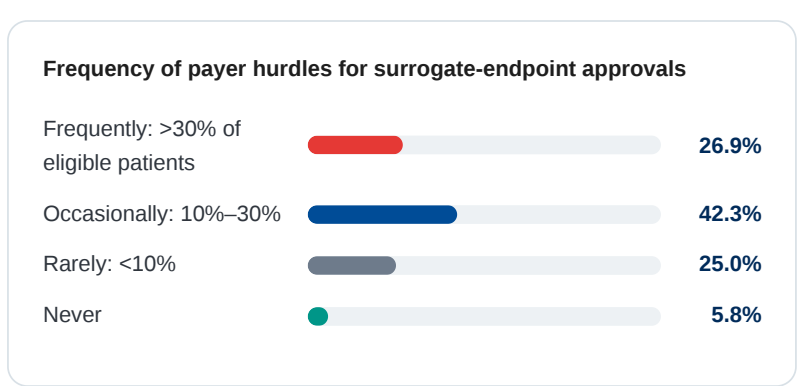
Among 52 respondents, 22 (42.3%) say reimbursement or prior-authorization hurdles occasionally affect 10%–30% of eligible patients, and 14 (26.9%) say the problem is frequent and affects more than 30%. Thirteen (25.0%) see such barriers rarely, while only three (5.8%) say payers in their region never restrict guideline-recommended drugs regardless of endpoint type. In Q15, 22 clinicians (43.1%) say mandatory real-world evidence tracking alongside confirmatory trials would most improve confidence in accelerated approvals. Requiring confirmatory trials to be fully enrolled or near completion and mandating automatic withdrawal after missed confirmatory endpoints each receive 23.5%; only 9.8% prefer no structural change.

THE INSIGHT

The evidence gap after accelerated approval is not only academic. It can become an access gap. Clinicians are often willing to use surrogate-based approvals, but payer friction can delay the treatment before the patient ever reaches the benefit-risk conversation. The preference for mandatory RWE suggests respondents want the post-approval evidence system to become more visible, continuous, and clinically interpretable rather than relying only on a later binary confirmatory readout.

WHY IT MATTERS

FDA Project Confirm emphasizes timely verification of benefit after accelerated approval, and current policy allows FDA to require confirmatory trials to be underway around the time of approval. For clinicians, confidence is strengthened when early access is paired with evidence that matures quickly and transparently. For patients, that same evidence may help reduce the disconnect between regulatory authorization and real-world coverage.


Frequency of payer hurdles for surrogate-endpoint approvals

09

FUTURE OF CLINICAL BENEFIT

Most respondents expect endpoint evolution, not the disappearance of OS

41.2% expect incremental change in which OS and PFS/EFS remain dominant while MRD and QoL stay secondary or exploratory; 37.3% expect a setting-specific shift.

CONTEXT

Precision oncology makes a single universal definition of benefit increasingly difficult. Molecular response may become decisive in one malignancy, organ preservation may matter most in another, and long survival after recurrence can make OS impractical in early-stage disease. The question is whether the field is heading toward a wholesale replacement of OS, a setting-specific hierarchy, or a slower expansion of supporting endpoints around the existing framework.

WHAT THE DATA SHOWS

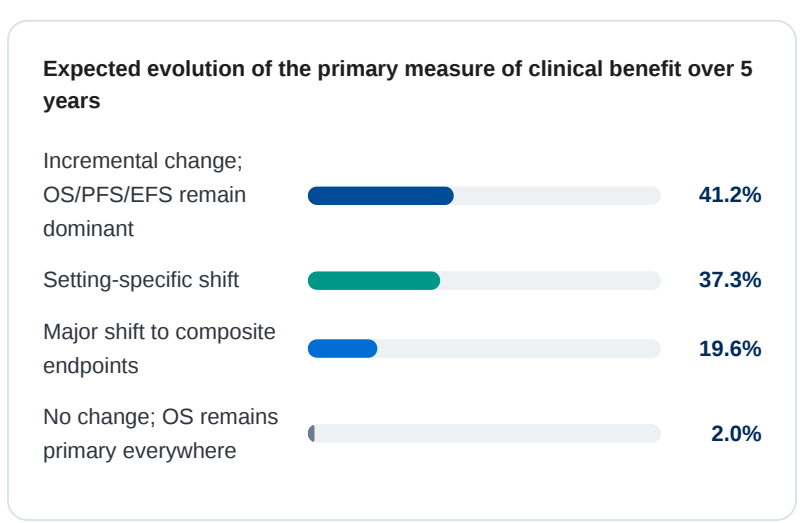
Among 51 respondents, 21 (41.2%) expect incremental change: OS and PFS/EFS will remain the dominant endpoints while MRD and QoL remain secondary or exploratory. Nineteen (37.3%) predict a setting-specific shift in which surrogate endpoints dominate early-stage or frontline settings while OS remains mandatory in relapsed or metastatic disease. Ten (19.6%) anticipate a major paradigm shift toward composite endpoints combining molecular response, organ preservation, QoL, and PFS/EFS as the primary benchmark across most malignancies. Only one respondent (2.0%) expects no change and strict OS primacy across all trial phases and disease settings.

THE INSIGHT

The future most clinicians imagine is plural. The two largest groups differ on the speed of change, but both retain a major role for established survival or disease-control endpoints. Only a small minority expect composite endpoints to replace OS broadly within five years, and almost no one expects the system to remain completely unchanged. That points toward a layered endpoint architecture rather than a new single gold standard.

WHY IT MATTERS

For trial design, regulatory review, guideline writing, and clinical communication, the challenge will be consistency. Earlier endpoints need disease-specific validation, standardized assays, and clear linkage to meaningful outcomes. Late endpoints such as OS still need rigorous assessment when they are secondary. And patient-centered outcomes need methods strong enough to influence the total benefit-risk judgment. The field is likely to become more contextual, but not less demanding about evidence.


Expected evolution of the primary measure of clinical benefit over 5 years

OPEN RESPONSE LENS

When clinicians say waiting for OS can harm care, they point to settings where time and treatment sequence distort the signal.

Q18 asked respondents for one scenario or disease setting where relying strictly on OS as a trial endpoint can harm patient care or delay access to innovation. Twenty visible responses span English, Italian, German, and French. A small number are non-specific, so the comments are treated as qualitative signals rather than coded percentages.

The responses do not converge on a single substitute for OS. Instead, they point to situations where long follow-up, treatment crossover and sequencing, disease-free control, molecular response, or symptom-focused goals can make mature OS slow to arrive or difficult to interpret. Because Q18 was not formally coded, these themes are presented as qualitative interpretation rather than prevalence estimates.

Long natural histories and early-stage disease

Respondents point to early-stage cancers, adjuvant or neoadjuvant therapy, and long natural histories where mature OS can take many years. High-risk early breast cancer is described as a setting where disease-free control may be meaningful long before mortality separates.

Hematologic malignancies

Multiple myeloma, AML, aggressive lymphoma, and long-survival blood cancers appear repeatedly. Comments emphasize that MRD, remission depth, bridging to transplant, or prolonged disease control can matter before OS matures.

Post-progression treatment and sequencing

Sequential treatment, including oncogene-addicted NSCLC, is cited as a setting where subsequent effective therapies can dilute the original treatment's OS signal. This makes earlier disease-control endpoints more interpretable in some scenarios.

Relapse prevention as clinical benefit

Several responses focus on preventing recurrence, organ damage, or disease complications rather than waiting for death as the only definitive outcome. The underlying argument is that avoiding relapse can itself be meaningful when the treatment burden is acceptable.

Advanced, oligometastatic, and palliative settings

Metastatic renal cancer, oligometastatic radiotherapy/SBRT, and advanced-stage scenarios appear in the comments. Here, PFS, symptom control, and treatment timing can influence care even when OS is confounded or slow to demonstrate.

Counterviews and limits

Not every response argues for earlier endpoints. Some comments say OS remains the gold standard or give no clear example. This minority perspective reinforces that endpoint flexibility is not the same as abandoning survival as the ultimate reference.

> What the open responses add: Clinicians are not saying OS is unimportant. They are identifying specific settings where waiting for mature OS can hide a meaningful earlier benefit, delay access, or make the original treatment's effect harder to see because later therapy changes the survival curve.

PEOPLE ALSO ASK · TOPIC FAQ

Frequently asked questions about oncology trial endpoints.

Is overall survival still the gold-standard endpoint in oncology trials?

Overall survival remains one of the most direct and important measures of clinical benefit because it measures how long patients live. However, oncology trials may also use validated earlier endpoints such as progression-free survival, event-free survival, response, disease-free survival, MRD, or other measures when the disease setting and evidence support them. FDA guidance increasingly addresses how OS should be assessed even when it is not the primary endpoint.

What is a surrogate endpoint in an oncology clinical trial?

A surrogate endpoint is a laboratory, imaging, response, or other measure expected to predict clinical benefit but that is not itself a direct measure of how a patient feels, functions, or survives. In oncology, examples can include response rate, PFS, DFS, EFS, or molecular-response measures, depending on the disease and regulatory context.

When can PFS or EFS be used instead of overall survival?

PFS or EFS may be appropriate when they are clinically meaningful, reliably measured, and suitable for the disease setting, especially when waiting for mature OS would take many years or be confounded by subsequent treatment. Whether they can support approval depends on the endpoint, effect size, trial design, disease context, and the totality of evidence.

Can MRD or ctDNA be used as an endpoint for cancer drug approval?

Potentially, but not universally. FDA has guidance on MRD in hematologic malignancies and ctDNA in early-stage solid-tumor drug development. A January 2026 draft guidance specifically addresses MRD and complete response as primary endpoints to support accelerated approval in multiple myeloma. Assay performance, disease setting, and validation remain critical.

How are patient-reported outcomes and quality of life used in oncology trials?

Patient-reported outcomes can capture symptoms, physical function, treatment burden, and health-related quality of life directly from patients. FDA issued final guidance in 2024 on a core set of PROs for cancer trials. Their regulatory weight depends on how they are measured, the trial design, and how they fit with efficacy and safety evidence.

What does accelerated approval mean for an oncology drug?

FDA accelerated approval can allow earlier access to a treatment for a serious condition based on a surrogate endpoint that is reasonably likely to predict clinical benefit. Confirmatory studies are required to verify that benefit, and an indication can be withdrawn if the expected benefit is not confirmed.

ONCOLOGY ENDPOINT DECISION LENS

What this means at four points between a trial readout and a treatment choice.

The survey suggests that endpoint interpretation works best when the clinician separates four questions: what the trial proved, what it did not prove, what the treatment will cost the patient in burden, and what outcome matters most in this clinical setting.

When reading a positive trial

Endpoint-fit lens. Ask whether the endpoint matches the disease setting, treatment intent, post-progression landscape, and time needed for OS to mature. A surrogate can be useful without being equivalent to OS.

When translating benefit to a patient

Benefit-risk lens. Put modest OS, PFS/EFS, chronic toxicity, performance status, and patient priorities into the same conversation. Statistical significance is only one part of clinical value.

When acting on MRD or ctDNA

Molecular-response lens. Distinguish validated disease-specific use from exploratory signal. Persistent negativity may support intensity reduction before it supports complete treatment cessation.

When access depends on uncertain evidence

Evidence-maturity lens. For accelerated or surrogate-based approvals, anticipate payer friction and track how confirmatory trials and real-world evidence change the strength of the original claim over time.

CLOSING PERSPECTIVE

The next oncology endpoint framework will probably be more contextual, not less rigorous.

The strongest message from the survey is not that oncologists want to abandon overall survival. It is that they already practice a hierarchy of evidence that changes with disease stage, natural history, molecular endpoint maturity, toxicity, patient goals, and access. OS remains the clearest direct endpoint, but respondents repeatedly identify settings where waiting for it can be slow, confounded, or poorly aligned with the decision that has to be made now.

That is why the largest Q7 group supports a setting-specific OS rule rather than universal primacy or wholesale demotion. It is why hematologic malignancies lead the MRD/ctDNA readiness question, yet persistent MRD negativity more often prompts dose or frequency reduction than complete treatment cessation. Clinicians appear willing to let earlier signals influence care before they are willing to treat every signal as a definitive replacement for clinical benefit.

The same caution appears around PFS/EFS. Most respondents accept a robust disease-control benefit without final OS, but the dominant stance is to prescribe with an explicit caveat that total lifespan has not been shown to improve. That distinction matters because PFS/EFS can prevent symptoms, organ damage, or relapse and still fail to translate into longer survival. The endpoint can be meaningful without carrying a stronger claim than the evidence supports.

Patient-reported outcomes reveal another layer. QoL is mostly secondary or supportive in the regulatory question, but symptom palliation and preserved function become the largest single driver of late-line shared decisions. In other words, the definition of "benefit" changes as evidence moves from population-level approval to individual patient care. Better trials may need to measure both dimensions rather than asking one endpoint to represent all of them.

Finally, accelerated approval does not end uncertainty. Payer hurdles are common enough to affect access, and respondents most often choose mandatory real-world evidence tracking as the policy change that would increase confidence. FDA's evolving framework around confirmatory trials, Project Confirm, and Project Endpoint makes this a live regulatory issue. Faster access and stronger verification have to work together if surrogate endpoints are to maintain trust.

1 · Match the endpoint to the disease setting

Interpret OS, PFS/EFS, MRD/ctDNA, and QoL according to treatment intent, natural history, crossover, and post-progression therapy.

2 · Separate statistical benefit from net clinical benefit

A modest survival gain should be weighed against chronic toxicity, function, age, performance status, and patient priorities.

3 · Use molecular response with disease-specific discipline

Let MRD or ctDNA inform decisions where validation is strong, but do not treat molecular negativity as a universal permission to stop therapy.

4 · Put function and symptoms into shared decisions

Late-line care may prioritize palliation and preserved daily function even when the pivotal trial was built around a survival endpoint.

5 · Anticipate the payer interpretation of surrogate evidence

Regulatory approval based on an earlier endpoint can still face coverage delays, so access planning is part of evidence translation.

6 · Keep post-approval evidence visible

Confirmatory trials and real-world evidence should progressively clarify what the early surrogate signal did and did not predict.

Help future oncology insights reflect how evidence is judged after the trial readout.

Join MDForLives to share clinical perspectives on trial endpoints, molecular response, toxicity, quality of life, access, and the evidence that changes practice.

Join the Panel

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