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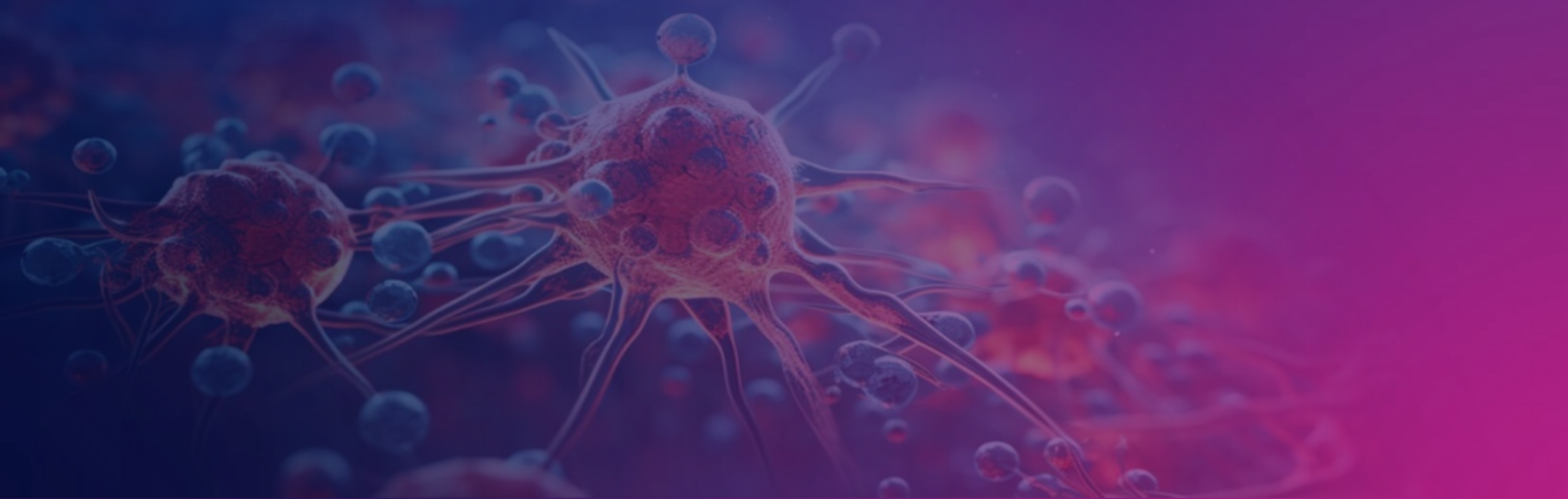
ASCO 2026

Key market shifts and considerations emerging from ASCO 2026



Signals of change in frontline NSCLC

The frontline NSCLC standard has been hard to shift. ASCO 2026 offered the clearest signs yet that this may be about to change. While these studies may not change practice yet, they start to shift how companies think about winning in frontline NSCLC - and whether IO / chemo-IO remains the benchmark to beat.

One of the most anticipated data sets of the meeting was **HARMONi-6** . The study showed an overall survival benefit for ivonescimab plus chemotherapy versus chemo-immunotherapy in frontline squamous NSCLC, establishing ivonescimab as a credible contender to the current treatment paradigm.

The result was met with both excitement and scrutiny, with questions remaining around follow-up duration, patient selection and applicability to global populations. Yet few disputed the significance of the finding itself: outperforming chemo-immunotherapy in frontline squamous NSCLC is one of the strongest signals yet that outcomes may be improved beyond today's benchmark.

HARMONi-6 wasn't the only dataset to turn heads. **OptiTROP-Lung05**, evaluating sacituzumab tirumotecan (Sac-TMT) plus pembrolizumab versus pembrolizumab alone in PD-L1-positive advanced NSCLC, also captured attention. While OS remains immature, the study reported a striking PFS benefit (HR 0.35).

But the discussion that followed raised an important question on the optimal route into frontline NSCLC for ADCs. Some programmes are betting on ADCs as a partner to immunotherapy in PD-L1-high disease, but will this prove more challenging than evolving existing chemo-IO approaches? Recent results from EVOKE-03 suggest so[1].

> “Ivonescimab, I’m sure, has been on everyone's watchlist, and this readout showed why. But how these results translate globally is still unclear, and that leaves a real planning question: how far do teams lean into this signal now versus waiting for global confirmation?

Siobhan

RAS gets its landmark moment

RASolute-304 delivered one of ASCO 2026's defining moments, with daraxonrasib doubling overall survival in second-line pancreatic cancer. The daraxonrasib result will be what ASCO 2026 is remembered for – but it also puts a spotlight on just how far RAS-targeted therapy has come and where we go from here.

Beyond establishing a new standard of care, the result shifts attention toward **what comes next** for RAS-targeted therapy. What started with mutant-selective KRAS (OFF)-state inhibitors has grown into a much wider field: ON-state inhibitors, pan-KRAS and pan-RAS approaches, degraders, tricomplex technologies, vaccines, and a growing list of combination strategies.

That breadth raises plenty of open questions. Does ON-state inhibition offer real gains in activity or tolerability over OFF-state approaches? Does targeting KRAS or RAS more broadly translate into longer-lasting responses by addressing resistance? And how much of the next leap forward will come down to combination strategies - and if so, which ones win out?

Not all the discussion was about new concepts, though. In NSCLC, **KRAS G12C inhibitors** have been striving to push into the frontline, though questions remain around combinability with immunotherapy and class-related toxicities such as hepatotoxicity. Data from elisrasib and divarasib shows continued appetite for this approach, but it's still not clear whether the path forward is about refining what we have - better dosing, better management - or something more fundamentally different.

> "The daraxonrasib data was one of those moments that just stays with you, showing how far the RAS field has come. What excites me looking ahead is the idea that pan-RAS and allele-specific approaches might come together to push outcomes further.

Kate

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ADCs: a call for payload diversification

This wasn't a year defined by a headline-grabbing ADC breakthrough. Yet ADCs remained central to discussions across ASCO, particularly what happens after ADC exposure, how should ADCs be sequenced, and what this means for ADC development?

Recent data offer some clues. The SATEEN study, presented shortly before ASCO, found that changing the target while retaining the same payload may offer limited benefit[2]. Interestingly, one of the datasets that attracted attention outside the main sessions was for LY4052031 in the post-EV setting in mUC; a space where, as EV moves earlier, the need for active subsequent options is only going to grow. Using the same target, Nectin-4, but switching the payload from MMAE to topo-I, showed encouraging activity, perhaps further supporting the notion that payload change may be a key component in ADC sequencing.

The challenge is that this raises a broader question for the field. More than 300 ADCs are currently in development, with a substantial proportion relying on topo-I payloads, and the oral abstract Developmental Therapeutics session reflected exactly that, with four ADC presentations, every one of them topo-I. In a separate session, one presenter called for an end to the **"tyranny of microtubule and TOP1 payloads"** among new entrants[3]. There are signs the field is listening; emiltatug ledadotin and emerging dual-payload ADCs suggest genuine interest in moving beyond classical payload classes. But, for topo-I ADCs still in early development, the competitive and sequencing environment may be more constrained than it once appeared.

> "With so many topo-I ADCs in development, it's getting harder to assume there's an obvious place for your asset. It forces a more honest look at where you actually want to play, and whether you can genuinely improve on what's already out there.

Paula

HR+ mBC: embracing complexity

ASCO 2026 opened and closed on the same theme in HR+ metastatic breast cancer: with an expanding range of options now in the mix, what treatment, or sequence of treatments, will keep a patient alive longest with the best possible quality of life? Clear positioning, and evidence generation, is important to guide where a therapy best fits in this complex landscape.

Part of this is about how patients are segmented. There's significant **heterogeneity** within "first-line" and "second-line" – not just in biomarkers, but in prior therapy and response, and the continuum that is endocrine sensitivity. Decision-making increasingly demands a more sophisticated framework, one that layers multiple inputs[4]. Trial design is starting to catch up: pionERA is built around a defined patient archetype rather than a broad line of therapy, helping identify where escalation of endocrine therapy brings most benefit.

Academics are also becoming more mindful of **sequencing** when evaluating new entrants. Questions were raised about endpoints intended to capture the value of sequencing strategies, such as PFS2, and whether they're robust enough to support the conclusions drawn from them. VIKTORIA-1 adds a further layer: despite a meaningful PFS benefit for comprehensive PAM pathway inhibition, this doesn't resolve whether that benefit is best delivered upfront or held back until after more selective PI3K-targeted therapy. It's not what the trial was built to test, but the fact that it's the question being asked says a lot about how central sequencing has become to how new data gets read.

> "There's a lot of academic enthusiasm for tailored sequencing in HR-positive breast cancer, but most oncologists on the frontline just want clear direction, not more complexity. That's a real question for brand teams: how do you actually deliver that clarity?

Kirsty

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Our team is always up for a conversation on the latest clinical developments and what they mean for pharma strategy. If you'd like to discuss we'd love to hear from you. Get in touch.

Paula Coyle
p.coyle@beyondblueinsight.com

Kate Goacher
k.goacher@beyondblueinsight.com

Siobhan Davies
s.davies@beyondblueinsight.com

Kirsty Hope
k.hope@beyondblueinsight.com

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