# Oncology Pulse

## Oncology's Red and Blue Oceans: Survival Gains vs. Persistent Gaps

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Bluestar BioAdvisors

*Strategic Experts in the Business of Life Sciences*

## By mapping the evolution of 1L standards of care across major solid tumors, we can systematically identify true areas of unmet need to focus future development

**Challenge**

**Identifying tumor types with high unmet medical need** in oncology requires a multi-dimensional analysis of clinical, regulatory, and market dynamics

**Framework and Approach**

Focused on ~15 top solid tumors and relevant sub-segments*

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Documented current vs. prior 1L SoC overall survival (OS)

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Categorized tumor types as "Red Ocean" vs. "Blue Ocean" based on magnitude of improvement and absolute OS



*Included patient segments with estimated 1L U.S. patients >7,000
Note: This analysis was conducted November 2025

# Despite the recent improvement in the SoC across the largest tumor types, more than half still have a mOS of <24 months signifying only incremental benefit in these indications

## Overall Survival Differential Between Old and New 1L SoC


Biomarker-driven segments (HER2+breast, HRD+ ovarian) and very IO-sensitive tumor types (melanoma, RCC) have experienced the biggest leaps in OS

Most tumor types benefited from IO, but gains remain largely confined to specific subgroups (e.g., non-squamous NSCLC, PD-L1–high TNBC)

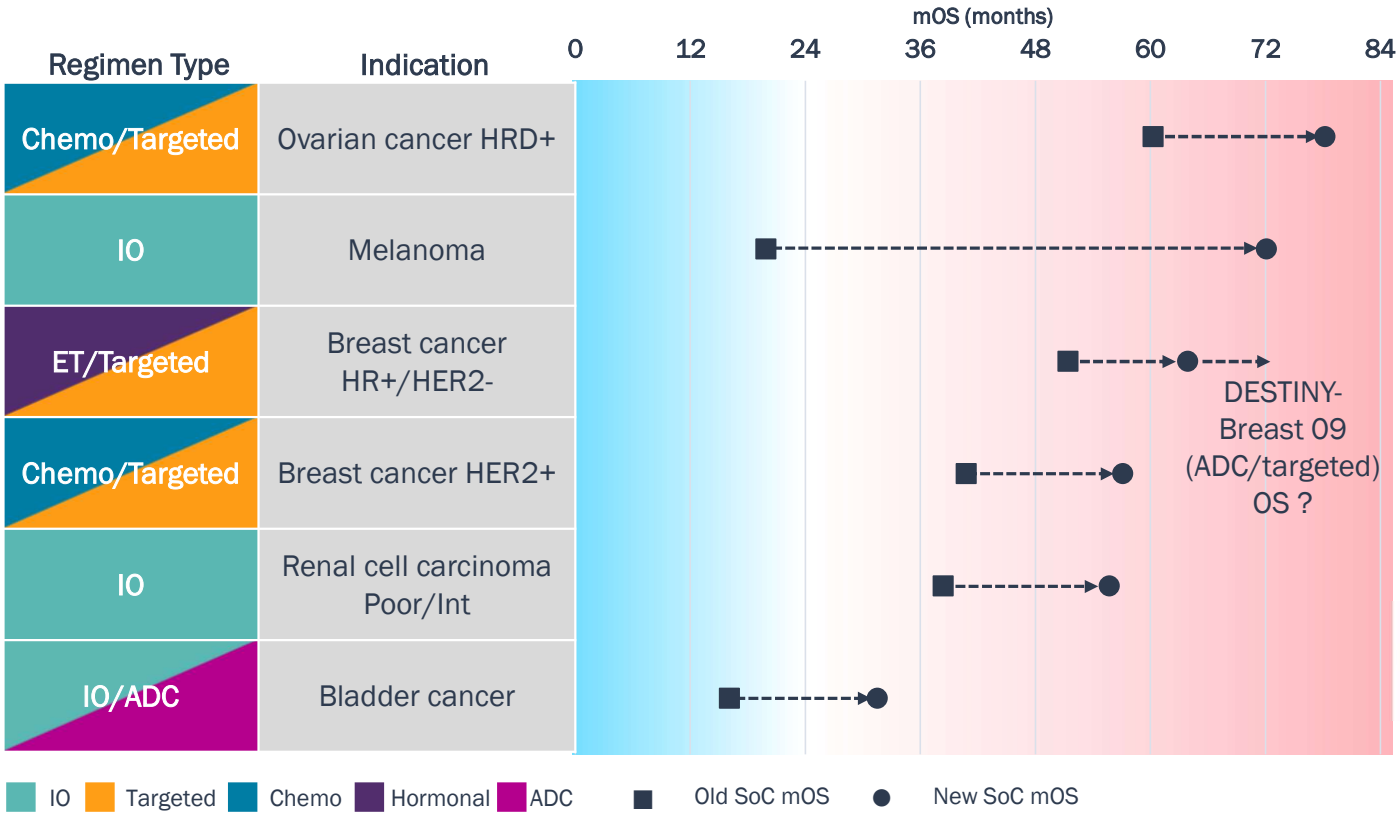
Absence of biomarkers to select treatment and no benefit from IO define many of these tumor types (e.g., CRC, mCPRC, PDAC)

The introduction of IO did not translate to a significant improvement in these tumor types compared to others

Abbreviations: NSCLC = Non-small cell lung cancer; TNBC = Triple-negative breast cancer; mCRPC = metastatic castration-resistant prostate cancer; GEA = Gastroesophageal adenocarcinoma; HNSCC = Head and neck squamous cell carcinoma; SCLC-ES = Small-cell lung cancer extensive stage; HRD = Homologous recombination deficient; NSq = Non-squamous; Sq = Squamous; pMMR = Mismatch repair proficient

# Even in “Red Ocean” tumors with strong 1L OS gains, opportunities remain to better identify poor responders and improve toxicity


## Red Ocean: ≥12 Months of Improvement in 1L SoC




- **Melanoma, renal cell carcinoma, and bladder cancer are the only tumor types with broad 1L regimens (no biomarker restriction),** all with IO-based SoC; melanoma in particular exemplifies IO’s potential
- **ADCs are beginning to reshape 1L therapy (e.g., EV in bladder cancer, T-DXd in HER2+ breast),** replacing chemo in key tumor types (e.g., cisplatin in bladder, taxane in HER2+ breast cancer)
  – Optimizing ADC use in 1L in terms of duration and combination regimens continues to evolve

**Toxicity with some MoAs** (e.g., CTLA-4, ADCs) and **sub-groups of refractory patients** highlight opportunities to improve tolerability and broaden benefit

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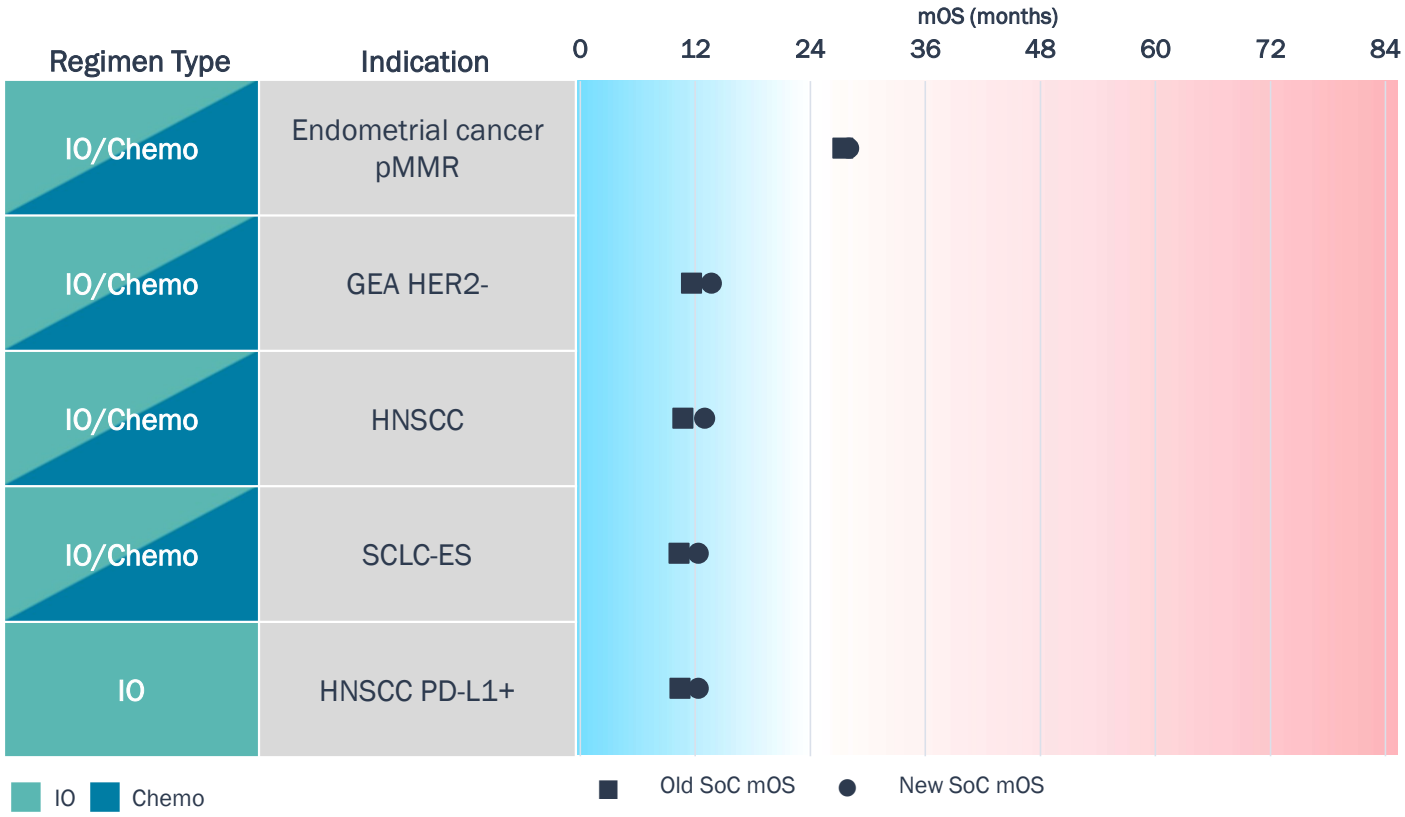
Targeted: ovarian (PARP); HR+/HER2- breast (CDK4/6); HER2+ breast (HER2)

# “Blue Ocean” tumors with the smallest 1L OS gains all rely on PD-1 based regimens, suggesting better patient selection and/or novel targets may help increase OS benefit

## Blue Ocean: <3 Months of Improvement in 1L SoC




- **All tumor types here have IO in 1L, but survival benefit is small**; most depend on PD-1 + chemo combination regimens
- **There is limited patient selection**– pMMR and HER2- are more representative of the residual patient pool left over after other targeted therapies

**Greater refinement in patient selection (biomarker-defined subgroups) and better targets suitable for these tumor types** could unlock more meaningful efficacy in these tumor types

# Recent 2025 ESMO conference highlighted not only the potential but also challenges of developing new targets and patient population selection strategies to address unmet needs

## Select ESMO 2025 Abstracts in "Blue Ocean" Tumor Types

| Drug (Target) | Tumor | Abstract | Key Takeaways |
|---|---|---|---|
| Bemarituzumab (FGFR2) | G/GEJC | Bemarituzumab (BEMA) + chemo for advanced or metastatic FGFR2b-overexpressing (G/GEJC): Ph3 FORTITUDE-101 results | Early OS benefit seen, but with longer follow-up **OS curves have converged. Unique corneal toxicity** seen that is reversible. **Ph3 FORTITUDE-102 (BEMA + chemo + nivo) also recently failed – unclear if similar toxicity issues persisted** |
| RC118 (CLDN18.2) | G/GEJC | RC118 (CLDN18.2-targeted ADC) + RC148 (PD-1/VEGF bispecific antibody) or PD-1 for previously treated locally advanced or metastatic G/GEJA | ADC + PD-1/VEGF demonstrated ORR 57.1% (vs. 33.3%) and mPFS 7.9mos (vs. 4.3 mos); **1L study for ADC + PD-1/VEGF planned could provide chemo free option for 1L CLDN18.2+** |
| Cadonilimab (PD-1/ CTLA-4) | G/GEJC | Cadonilimab (Cado) + chemo vs. chemo as 1L G/GEJA : final results Ph3 COMPASSION-15 trial | **Cadonilimab by Akeso is already approved in China** for 1L G/GEJC; final analysis **confirms long-term OS benefits, esp. in PD-L1 low-neg groups** |
| Tarlatamab (DLL3xCD3) | ES-SCLC | Tarlatamab with first-line chemo-IO for ES-SCLC: DeLLphi-303 study | **mOS of 25.3 mos** from start of maintenance for tarlatamab + PD-1 with **low grade CRS and ICANS; Ph3 DelIPhi-305 is ongoing** |
| Enfortumab vedotin (Nectin-4) | HNSCC | Enfortumab vedotin plus pembrolizumab as 1L in R/M HNSCC: results from a cohort in EV-202 trial | **ORR of 39% in 41 patients**, mOS not reached; trial enrolled CPS ≥1 patients |

*While not at ESMO, there was considerable buzz about Genmab/Merus's Petosemtamab (EGFRxLGR5 bispecific) in HNSCC which is in Ph3 for 1L PD-L1+ HNSCC; previous Ph2 data showed 63% ORR and 9 mos mPFS*

Source: ESMO 2025 Abstract Titles

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