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Clarivate's top takeaways from ASCO 2026

Market Event Summary

Joan Tur, Ph.D. | June 2026

Perioperative Erleada improves pCR/MRD and MFS in high-risk prostate cancer

Context

- High-risk localized prostate cancer remains associated with a substantial risk of recurrence despite curative-intent treatment.
- Building on the proven benefit of androgen receptor pathway inhibitors (ARPIs) in advanced disease, the Phase 3 **PROTEUS** trial evaluated perioperative Erleada plus androgen deprivation therapy (ADT) vs. perioperative ADT alone in patients undergoing radical prostatectomy.

Key findings

- Pathological complete response or minimal residual disease (pCR/MRD; co-primary endpoint) was achieved in 8.9% vs. 1.0% of patients (odds ratio 10.17; $P < 0.001$).
- Metastasis-free survival (MFS) by conventional imaging or PSMA PET (co-primary endpoint) was significantly longer in the Erleada arm (5-year MFS rates: 78.2% vs. 73.5%; HR 0.80; $P = 0.02$). However, MFS assessed by conventional imaging alone was not significantly improved (HR 0.84; $P = 0.15$).
- Grade 3/4 treatment-related adverse events (TRAEs) were more frequent in the Erleada group (27.5% vs. 18.9%), driven largely by rash. FatalTRAEs occurred in 0.7% vs. 0.1% of patients.

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Clarivate's takeaways

Potential new standard of care

PROTEUS met both co-primary endpoints, and Clarivate expects Johnson & Johnson to seek approval for perioperative Erleada plus ADT based on these data. We anticipate this approach will become a new standard of care for high-risk localized prostate cancer patients selecting surgical management.

Efficacy effect size raises doubts

The magnitude of the MFS benefit was modest and depended on PSMA PET–detected events, an endpoint not yet validated as a survival surrogate. No significant improvement was observed in conventional-imaging MFS. In addition, the absolute pCR/MRD rate remained low despite a large relative improvement over control.

Uptake will likely be selective

If approved, uptake is likely to concentrate among fit, very-high-risk surgical candidates, where the highest absolute recurrence risk may make the modest benefit more relevant. Radiotherapy plus ADT and prostatectomy followed by selective salvage radiotherapy will likely remain key alternatives.

Adjuvant Retevmo improves EFS in resectable *RET*-positive NSCLC

Context

- Early-stage non-small-cell lung cancer (NSCLC) is treated with curative-intent resection plus (neo)adjuvant systemic therapy.
- Although targeted agents are available for EGFR- and ALK-positive disease, and immunotherapy for wild-type disease, no targeted agents are currently approved for early-stage NSCLC with *RET* fusions.
- The Phase 3 **LIBRETTO-432** trial in stage IB-IIIA NSCLC assessed adjuvant treatment with the RET inhibitor Retevmo, which is currently approved for *RET*-fusion positive metastatic NSCLC. In February 2026, Eli Lilly reported that the trial met its EFS primary endpoint.

Key findings

- The investigator-assessed event-free survival (EFS) rate at 24 months in the stage II-IIIA primary analysis population was 91.5% for Retevmo versus 61.1% for placebo (HR 0.17, P = 0.0003). The median EFS was not reached for Retevmo, and it was 31.8 months for placebo.
- Overall survival (OS) data were immature, with no deaths in the Retevmo group versus three in the placebo group.
- Grade ≥3 AEs occurred in 66.7% vs. 23.7% of patients, serious AEs in 22.7% vs. 13.2%, and AEs leading to discontinuation in 17.3% vs. 1.3%. No fatal AEs were reported.

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Expected approval and practice-changing potential

Clarivate expects the impressive EFS improvement shown in **LIBRETTO-432** to secure regulatory approval and be practice-changing in stage II-IIIA resectable *RET*-positive NSCLC.

Lack of competition

If approved, Retevmo is unlikely to face competition from other RET inhibitors in the resectable setting during the forecast period, positioning it as the leading targeted option in this biomarker-defined population.

Biomarker testing will constrain uptake

Identification of eligible patients will be critical for uptake, as *RET* fusion testing is not yet routine in early-stage NSCLC in real-world practice.

STRIDE-based regimens challenge TACE alone in unresectable eeHCC

Context

- Transarterial chemoembolization (TACE) has been the standard of care for unresectable embolization-eligible hepatocellular carcinoma (eeHCC), but median progression-free survival (PFS) is typically only around 8 to 10 months. Attempts to combine TACE with immunotherapy have not delivered convincing benefit thus far.
- Following the improved survival observed with the STRIDE regimen (single tremelimumab regular interval durvalumab) in advanced HCC (HIMALAYA trial), **EMERALD-3** investigates whether adding STRIDE, with or without Lenvima, to TACE extends disease control in unresectable eeHCC.

Key findings

- STRIDE + TACE + Lenvima (arm A) improved PFS ~~(arm A)~~ versus TACE alone (arm C) (13.0 vs. 9.8 months; HR 0.70; P = 0.007) and showed a favorable OS trend (median: 39.5 vs. 34.7 months; HR 0.84; P = 0.18).
- Although not formally compared, STRIDE + TACE (arm B) vs. TACE alone delivered a similar PFS improvement (12.9 vs. 8.1 months; HR 0.71; P = 0.0062) and early OS trend (HR 0.70).
- While safety was consistent with known drug profiles, treatment discontinuation due to AEs was substantial with STRIDE-containing approaches, particularly in the triplet arm (35.5% for arm A and 20.6% for arm B).

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Clarivate's takeaways

Long-standing TACE paradigm disrupted

EMERALD-3 is among the first Phase 3 trials in unresectable eeHCC to show clinically meaningful improvements over TACE alone after years of largely negative combination studies, supporting a potential role for STRIDE-based regimens in this setting.

Lenvima's added value remains uncertain

In the absence of a formal comparison in this analysis, the added value of Lenvima remains uncertain, as STRIDE + TACE achieved a similar PFS benefit to STRIDE + TACE + Lenvima with a better safety profile.

Commercial upside hinges on OS benefit

Despite encouraging PFS and response data, mature OS results remain critical to determine whether STRIDE-based approaches can meaningfully reshape treatment, particularly given substantial discontinuation rates.

PersevERA trial misses PFS in first-line ER-positive / HER2-negative metastatic breast cancer

Context

- Giredestrant is an oral selective estrogen receptor degrader (SERD) being developed across multiple treatment settings in ER-positive / HER2-negative breast cancer.
- The Phase 3 **persevERA** trial tested giredestrant plus Ibrance as first-line treatment for endocrine-sensitive locally advanced or metastatic disease, using the standard-of-care letrozole plus Ibrance as the comparator. However, in March 2026, Roche announced that this trial did not meet its primary endpoint of investigator-assessed PFS.

Key findings

- At a median follow-up of 52.2 months, giredestrant plus Ibrance did not demonstrate a statistically significant PFS benefit compared with letrozole plus Ibrance (investigator-assessed median PFS: 33.1 months vs 28.2 months; HR 0.89, P = 0.1553). A trend towards greater benefit among patients without visceral metastases was observed.
- OS data were immature but not significantly different between arms (HR 1.03, P = 0.7767), with overall response rate (ORR) and clinical benefit rate (CBR) similar between giredestrant plus Ibrance and letrozole plus Ibrance arms (ORR: 60.2% vs. 58.8%; CBR: 82.6% vs. 82.1%).

Clarivate's takeaways

Frontline metastatic strategy under pressure

Clarivate anticipates these findings will impact Roche's efforts to move giredestrant to frontline metastatic use. The negative outcome also raises questions for mechanistically similar oral SERD plus CDK4/6 inhibitor combinations, most notably camizestrant plus Ibrance in SERENA-4, expected to read out in H2 2026.

Metastatic role narrows to resistant disease

Roche´s U.S. regulatory filing is under review for ESR1-mutated later-line metastatic disease, supported by the PFS benefit observed in the Phase 3 evERA trial. These positive data highlight a role for giredestrant in endocrine-resistant metastatic disease, where unmet need remains high and differentiation versus existing therapies is more achievable.

Strategic focus shifts toward early-stage disease

The failure of the **persevERA** trial, alongside positive lidERA results, signals a shift for giredestrant toward early-stage breast cancer. Notably, giredestrant is the first oral SERD to demonstrate a clinically significant adjuvant benefit based on Phase 3 lidERA data, strengthening its positioning in early-stage disease.

Mezigdomide in combination with Kd significantly improves PFS in R/R multiple myeloma

Context

- Mezigdomide is an oral cereblon E3 ligase modulator (CELMoD) agent being developed by Bristol Myers Squibb (BMS) as part of its lifecycle management strategy to replace Imnovid/Pomalyst in relapsed or refractory (R/R) multiple myeloma.
- The Phase 3 **SUCCESSOR-2** trial is evaluating mezigdomide in combination with Kyprolis and dexamethasone (Mezi-Kd) vs. Kyprolis and dexamethasone (Kd). In March 2026, BMS announced that SUCCESSOR-2 met its primary endpoint of PFS.

Key findings

- Median PFS was 18.0 months with Mezi-Kd vs. 8.3 months with Kd (HR 0.48, P < 0.0001). Additionally, PFS was significantly improved across all prespecified subgroups, including patients refractory to anti-CD38 monoclonal antibodies and lenalidomide.
- At the time of this interim analysis, OS data were immature; however, a positive OS trend was observed, favoring Mezi-Kd (HR 0.79).
- Grade 3/4 treatment-emergent adverse events (TEAEs) were more frequent with Mezi-Kd vs. Kd (83.7% vs. 56.5%).

Clarivate's takeaways

Regulatory path forward

BMS plans to share positive interim PFS results from **SUCCESSOR-2** with global regulatory agencies, and Clarivate expects Mezi-Kd to receive FDA approval in 2027.

Expanding the R/R multiple myeloma armamentarium

Mezi-Kd could expand treatment options in R/R multiple myeloma, particularly for the growing population refractory to an anti-CD38 monoclonal antibody and/or lenalidomide. If approved, Clarivate anticipates strong uptake despite intense competition.

Kd control arm undermines potential efficacy benefit

Despite positive interim PFS data, the trial's design may be considered controversial due to the use of Kd as the control arm, comparing a triplet versus a doublet regimen. In addition, Kd is not listed as a preferred regimen in NCCN guidelines but as an option which can be used in certain circumstances only.

Clarivate coverage of relevant indications

Prostate cancer

- Disease Landscape & Forecast | G7 countries
- Epidemiology | Global markets including G7 countries
- Current Treatment | US
- Unmet Need | US and Europe
- China In-Depth | China

Non-small-cell lung cancer

- Disease Landscape & Forecast | G7 countries
- Epidemiology | Global markets including G7 countries
- Current Treatment | US
- Unmet Need | US and Europe
- China In-Depth | China

Hepatocellular carcinoma

- Disease Landscape & Forecast | G7 countries
- Epidemiology | Global markets including G7 countries
- Unmet Need | US and Europe
- China In-Depth | China

Breast cancer

- Disease Landscape & Forecast | G7 countries
- Epidemiology | Global markets including G7 countries
- Current Treatment: Physician Insights | US
- Treatment Sequencing | US
- Unmet Need | US and Europe
- China In-Depth | China

Multiple myeloma

- Disease Landscape & Forecast | G7 countries
- Epidemiology | Global markets including G7 countries
- Current Treatment | US
- Unmet Need | US and Europe
- China In-Depth | China

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