Carelon Medical Oncology Program Q1 2026 Pathway Updates

The Q1 2026 external advisory panel (Feb 10, 2026) focused on a targeted set of high-impact literature updates and operational questions from OPEC, with an explicit goal of aligning Pathways with credible, practice-changing evidence while preserving clinical flexibility where uncertainty remains. Across tumor types, the panel repeatedly applied the same decision rubric: (1) strength and maturity of benefit (OS > EFS/PFS > surrogate endpoints), (2) generalizability and subgroup robustness, (3) toxicity/cost tradeoffs, and (4) anticipated impact on real-world adoption and pathway adherence.

Program context and "why this quarter mattered"

Two themes framed the meeting: information overload in oncology practice and the need for pragmatic tools that reduce friction without suppressing clinical judgment. The panel reviewed the continuing improvement in pathway adherence from 2024 to 2025, recognizing that both workflow improvements and denominator management contribute to this trajectory.

Breast cancer

Metastatic HER2-positive disease: add (don't replace) T-DXd + pertuzumab

The panel reviewed interim data from DESTINY-Breast09 evaluating trastuzumab deruxtecan (T-DXd) plus pertuzumab against taxane/trastuzumab/pertuzumab (THP) in the first-line metastatic setting. The interim results showed a large PFS signal (median PFS 40.7 vs 26.9 months; HR ~0.56), with higher response rates and longer duration of response, but with meaningful ILD/pneumonitis risk (including rare fatal events). The panel also noted that the magnitude of benefit scoring (ESMO MCBS grade 3) reflected reliance on PFS at this time and ongoing uncertainty about OS, long-term tolerability, and optimal duration/de-escalation strategies.

Decision: add T-DXd + pertuzumab as an additional first-line pathway option for stage IV/recurrent HER2+ breast cancer, but **do not** remove existing taxane-HP options. The core logic was: the PFS advantage is clinically compelling and adoption is increasing; however, unresolved OS durability, ILD risk in a potentially long "maintenance-like" exposure window, and heterogeneity across HR+/HR– subgroups argue against making it the default for all patients.

Neoadjuvant HER2-positive early breast cancer: promising pCR, but wait for EFS/approval

DESTINY-Breast11 tested an anthracycline-sparing approach (T-DXd→THP) versus ddAC→THP in high-risk HER2+ early breast cancer. It demonstrated a statistically significant pCR improvement (absolute pCR increase ~11%), with EFS still immature at the time of review. (Harbeck N, Ann Oncol, 2025).

Decision: no pathway change yet. The panel's consistent position was that pCR—while useful—does not automatically justify pathway inclusion absent mature EFS and clear regulatory/professional society alignment.

Post-neoadjuvant residual invasive HER2-positive disease: add T-DXd as an option, keep T-DM1 for now

The panel reviewed phase 3 data from DESTINY-Breast05 comparing adjuvant T-DXd versus T-DM1 in patients with residual invasive HER2+ disease after neoadjuvant therapy, showing a substantial improvement in invasive DFS (HR ~0.47). The trial's benefit magnitude (curative-intent context) supported strong consideration for elevating T-DXd. At the same time, the panel emphasized practical implementation: higher toxicity burden and cost versus T-DM1, plus guideline positioning that (at the time) focused on specific high-risk subgroups.

Decision: add T-DXd as an additional pathway option in the "adjuvant HER2+ residual disease" scenario, while **retaining T-DM1** as a pathway option pending further FDA and guideline evolution.

Endocrine (metastatic) and ESR1 mutations: keep out of scope—for now

The panel revisited EMBER-3 and the emergence of multiple ESR1-directed endocrine options. The primary EMBER-3 publication demonstrated improved PFS for imlunestrant versus standard endocrine therapy in ESR1-mutated disease (with OS still immature), and also showed improved PFS for imlunestrant + abemaciclib versus imlunestrant. (Jhaveri KL, N Engl J Med, 2024). (Prof. Elgene Lim)
Despite FDA approval and NCCN inclusion for imlunestrant, the panel emphasized a key "Pathways scope" principle: new scope is most justified when there is a clearly superior choice that simplifies (rather than complicates) decision-making. Here, ESR1-targeted choices compete with other biomarker-driven options (e.g., PIK3CA/AKT pathway decisions), and relative sequencing is not settled.

Decision: no change; ESR1-mutated HR+ metastatic breast cancer remains out of scope for a dedicated second-line endocrine pathway scenario at this time. The panel also noted that camizestrant updates (SERENA program) did not warrant change because of lack of the necessary regulatory/guideline positioning at the time of review.

Urothelial carcinoma (bladder)

Create/clarify perioperative pathway structure; add EV/pembro, add NIAGARA regimen, add adjuvant nivolumab scenario

This was the most structurally "pathway-changing" section of Q1 2026, because the panel addressed **three** peri-/adjuvant decision points and used them to refine scenario architecture.

1) Cisplatin-ineligible MIBC: add perioperative enfortumab vedotin + pembrolizumab
KEYNOTE-905/EV-303 demonstrated major improvements in EFS and OS versus surgery alone, with a striking increase in pCR, but also with substantial grade ≥3 toxicity and a need for careful perioperative risk management. (Vulsteke C, N Engl J Med, 2026).
Decision: add EV + pembrolizumab to a newly clarified "neoadjuvant/perioperative therapy" scenario for stage IIA–IVA (M0), explicitly capturing the cisplatin-ineligible population.

2) Cisplatin-eligible MIBC: re-evaluate and add NIAGARA "sandwich" durvalumab + GC → cystectomy → adjuvant durvalumab
NIAGARA showed significant improvements in EFS and OS versus neoadjuvant GC and cystectomy alone. (Powles T, N Engl J Med, 2024).
This quarter's decision differed from the earlier (Q4 2024) discussion because the evidence

matured in the real world: FDA approval (Mar 28, 2025) and broader professional positioning reduced implementation ambiguity.
Decision: add perioperative durvalumab + gemcitabine/cisplatin followed by adjuvant durvalumab to the same clarified perioperative scenario (stage II–IVA, M0), avoiding unnecessary scenario proliferation while reflecting practical treatment selection by eligibility.

3) Adjuvant therapy after radical resection: add nivolumab based on mature survival data
The panel highlighted that adjuvant immunotherapy is no longer a theoretical question: CheckMate 274 established DFS benefit initially (Bajorin DF, N Engl J Med, 2021), and longer follow-up has continued to support durable DFS improvement with emerging OS trends and ctDNA-stratified insights. (Galsky MD, Ann Oncol, 2026).
Decision: create a **new adjuvant therapy** scenario (stages II–IVA after radical resection) and add nivolumab as a pathway option—closing an important gap in the current bladder pathway structure.

Hematologic malignancies

Mantle cell lymphoma: ENRICH reviewed, but chemo-free IR not added

ENRICH compared ibrutinib + rituximab versus immunochemotherapy (R-CHOP or BR) in untreated MCL patients ≥60. While PFS improved overall, the panel emphasized that the benefit signal was not uniform across the chemo comparator choices and that the regimen introduces BTK-inhibitor toxicities and cost/monitoring considerations. (Lewis DJ, Lancet, 2025).
Decision: do not add ibrutinib + rituximab as an on-pathway first-line option for ASCT-ineligible disease at this time.

Multiple myeloma: resolve OPEC operational questions; tighten scope; selectively add high-impact 2L innovation

This segment blended "how Pathways is measured" with evidence review.

Operational decisions (OPEC-driven):

- **Transplant is not a line of therapy** for pathway purposes; add a clarifying footnote.
- **Second-line remains in scope; third-line will not be added** (complexity and attrition make reliable pathway assignments harder in later lines).
- **Maintenance therapy removed from scope** (low observable utilization through the pathway authorization workflow and limited value for pathway accountability).

Evidence-based regimen decisions:

- **Isatuximab-RVd (GMMG-HD7):** not added—MRD-driven signals were viewed as insufficiently practice-defining without OS/maintenance outcomes and with cost concerns.
- **D-VRd (CEPHEUS):** not added—despite deep response/MRD signals, the panel did not view it as sufficiently simplifying or clearly superior within the current pathway architecture for transplant-ineligible/deferred NDMM.
- **MajesTEC-3 (teclistamab + daratumumab): added** to second-line options because it is a rare example of an "off-the-shelf" immunotherapy combination showing a substantial

efficacy advantage early in the relapsed setting. The panel also removed the "early relapsed disease" label to reduce ambiguity and better reflect real-world treatment selection. (Costa LJ, N Engl J Med, 2026).

DLBCL: POLARIX 5-year data reviewed; keep R-CHOP as the pathway position

POLARIX five-year outcomes continued to show a modest PFS advantage but **no statistically significant OS benefit,** and the panel felt that reliance on non-prespecified subgroup interpretations (e.g., non-GCB or other high-risk biology) should not drive a pathway-wide default absent widely available predictive biomarkers. (Morschhauser F, J Clin Oncol, 2025).
Decision: maintain current pathway (R-CHOP); pola-R-CHP remains off-pathway.

Lung cancer

SCLC: bring second-line into scope; add tarlatamab

DeLLphi-304 demonstrated a clinically meaningful OS improvement for tarlatamab versus chemotherapy in second-line SCLC after platinum (median OS 13.6 vs 8.3 months; HR ~0.60). (Mountzios GS, N Engl J Med, 2025).
Decision: create a new second-line SCLC scenario and add tarlatamab. The panel explicitly framed this as a "awareness enhancing" intervention to reduce defaulting to older, less effective options (e.g., topotecan) when a superior therapy exists.

Tumor types reviewed without changes

Follicular lymphoma and uterine cancer were reviewed without new literature-driven pathway changes in Q1 2026.

Bottom line for participating oncologists

Q1 2026 resulted in **targeted additions** where evidence is strong enough to warrant pathway steering (perioperative bladder regimens; adjuvant nivolumab; second-line SCLC tarlatamab; second-line myeloma teclistamab+daratumumab; first-line metastatic HER2+ breast T-DXd+pertuzumab as an option), and **intentional restraint** where endpoints are immature, OS is not established, or heterogeneity makes a single pathway default potentially misleading.