Carelon Medical Oncology Program Q2 2026 Pathway Updates:

The Q2 2026 Carelon Oncology Pathways panel reviewed six tumor-specific pathway areas—gastroesophageal, biliary, hepatocellular, melanoma, kidney, and CML—and one focused review in multiple myeloma. In this brief review, the goal is to highlight some of the overarching issues that were discussed, and also summarize some of the specific pathway topic discussions in an effort to highlight some of the new data reviewed and the basis for various pathway decisions.

The meeting was framed by an operational update showing continued improvement in overall pathway adherence, now approaching 60% in 2026. The panel also discussed the emerging ESMO EnLiST framework for standardizing lines of systemic therapy, recognizing that inconsistent line-of-therapy assignment is a frequent source of ambiguity in pathway operations, utilization management, and retrospective review.

Gastroesophageal cancer: two key updates

1) *PD-L1 threshold lowered for 1L chemoimmunotherapy (HER2-negative)*

Change: For HER2-negative locally advanced/metastatic/recurrent gastroesophageal cancer, the PD-L1 **CPS threshold for on-pathway first-line chemoimmunotherapy is now CPS ≥1 (previously CPS ≥5).
Why this changed:

- Longer-term follow-up from CheckMate 649 (Janjigian YY, Ann Oncol, 2026) continues to show an overall survival benefit for nivolumab + fluoropyrimidine/platinum, including across CPS subgroups (with larger benefit at higher CPS).
- The updated ASCO guideline (Shah MA, J Clin Oncol 2026) supports immunotherapy + doublet chemotherapy for HER2-negative disease with PD-L1 CPS ≥1, while noting that higher PD-L1 expression is associated with greater likelihood of benefit.

Panel rationale: Keeping the CPS cutoff at 5 risks sending the wrong message clinically (that CPS 1–4 patients "shouldn't" receive chemoimmunotherapy), even though the benefit is smaller in that group. The panel unanimously supported moving the on-pathway threshold to CPS ≥1.

2) Perioperative "sandwich regimen" clarified for durvalumab + FLOT
Change: The pathway now reflects the full perioperative regimen from MATTERHORN (Janjigian YY, NEJM 2025):

- Neoadjuvant durvalumab + FLOT, then surgery, then
- Adjuvant durvalumab + FLOT, followed by
- Durvalumab monotherapy.

Important footnote: This adjuvant pathway option is intended only for patients who started the regimen preoperatively, consistent with the trial design (perioperative evidence, not "pure adjuvant" evidence).
Administrative alignment for HER2-positive disease
The panel also accepted (administratively) adding FOLFOX + pembrolizumab + trastuzumab for unresectable HER2-positive CPS ≥1 disease to align with an existing on-pathway option (CAPOX + pembrolizumab + trastuzumab).

Biliary tract cancers: no changes this quarter

No Q2 additions, removals, or sequencing changes were made in biliary tract cancers. This section was essentially a status review.

Hepatocellular carcinoma (HCC): updated data reviewed, but no pathway change
The panel reviewed longer follow-up from CheckMate-9DW presented at the 2026 ASCO GI Symposium (Galle PR, J Clin Oncol abstract, 2026) comparing nivolumab + ipilimumab vs investigator's choice lenvatinib or sorafenib in untreated unresectable HCC. The updated results continued to show an OS advantage and durable responses.
Decision: Nivolumab + ipilimumab remains off-pathway in the first-line setting.
Why: This was a value/comparator issue, not an efficacy issue. The trial compared against TKIs—not against atezolizumab + bevacizumab, which remains the leading first-line on-pathway option with strong adoption, mature efficacy data, and favorable patient-reported outcomes. The panel also noted dual immunotherapy cost and lack of a clear quality-of-life or toxicity advantage.

Melanoma: RELATIVITY-047 long-term update reviewed, no change
Some physicians asked whether longer-term RELATIVITY-047 results should change the pathway status of nivolumab–relatlimab in first-line metastatic cutaneous melanoma.
What the panel saw: 4-year follow-up (Lipson EJ, Eur J Cancer, 2025) showed stable longer-term outcomes, with maintained PFS/ORR advantages vs nivolumab alone, numerically higher OS, and no new safety signals.
Decision: No pathway change. Ipilimumab–nivolumab remains the on-pathway combination immunotherapy choice, and nivolumab–relatlimab is not added at this time.
Why: The panel felt the "less toxic than ipi/nivo" argument is not yet compelling enough in magnitude and scope, quality-of-life advantage is not clear, there's no head-to-head comparison with ipi/nivo, and ipi/nivo still has more mature long-term survival data and a stronger evidence base in CNS disease.

Kidney cancer: no pathway changes
The panel reviewed recent RCC guideline updates and contemporary reviews but identified no new trial evolution or evidence changes requiring pathway modification. First-line emphasis remains on established I/O–TKI combinations (eg, nivolumab/cabozantinib; pembrolizumab/axitinib).

CML: asciminib data reviewed, no pathway change
The panel reviewed the 96-week ASC4FIRST update (asciminib vs investigator-selected TKIs) in newly diagnosed chronic-phase CML, which continued to show improved molecular responses and favorable tolerability (Cortes JE, Blood, 2026).
Decision: No pathway change.
Why: CML treatment is often long-term (years). The panel felt that response/tolerability improvements have not yet translated into an overall survival benefit or a mature long-term value case sufficient to change initial pathway strategy. Based on the current evidence, the preferred approach remains: start with a lower-cost TKI and switch based on tolerability/response, pending more mature data.

Multiple myeloma (transplant-ineligible): key clean-up on lower-intensity options

The Q2 panel revisited first-line therapy for transplant-ineligible patients and reaffirmed that daratumumab-VRd (CEPHEUS, Usmani SZ, Nat Med, 2025) would not be added. The panel also noted that isatuximab-VRd (IMROZ, Facon F, NEJM 2024) represents a quadruplet on pathway with strong phase 3 PFS data in transplant-ineligible newly diagnosed disease.
Major Q2 action: removing legacy lower-intensity regimens from pathway
Removed from on-pathway first-line options (transplant-ineligible):

- CyBorD/VCD
- Rd
- Vd

Why: The panel felt current standards have shifted toward triplets and quadruplets with stronger evidence and better overall value. Lower-intensity options and CyBorD may still be reasonable for selected frail or clinically complex patients, but the panel preferred these remain available off-pathway as individualized choices rather than being positioned as optimal default regimens.

Looking ahead
The next formal review is planned for Q3, as the panel digests new data expected from the ASCO Annual Meeting (May 31–June 3).