



Carelon Medical Oncology Program Q 3 2026 Pathway Updates:

Carelon Oncology Pathways are intended to promote appropriate, safe, affordable cancer care by identifying evidence-based regimen choices that offer strong clinical value for common oncology scenarios. The Q3 2026 pathway review on July 28, 2026 covered mantle cell lymphoma, CLL/SLL, multiple myeloma, metastatic breast cancer, prostate cancer, bladder cancer, ovarian cancer, and colorectal cancer. The panel discussion emphasized a familiar theme: new evidence matters, but pathway decisions also depend on toxicity, patient burden, affordability, operational feasibility, and whether the clinical scenario can be implemented reliably in the program workflow.

The bottom line is that several pathway changes were made, but not every new study warranted a change. Some decisions added new regimens because the clinical benefit was meaningful and the evidence was mature enough. Other decisions removed outdated options, clarified line-of-therapy scope, or refined workbook language so that pathway adherence better reflects real clinical practice.

Mantle cell lymphoma

What changed: The first-line mantle cell lymphoma pathway is being reframed around TP53 wild-type disease and suitability for aggressive versus less aggressive induction therapy. Alternating R-CHOP/R-DHAP without ibrutinib is being removed from first-line pathways. The ibrutinib-containing TRIANGLE induction approach using the study Arm I regimen (alternating R-CHOP+ibrutinib with R-DHAP or R-DHAox/R-DHAX) is being added for patients with stage II-IV, TP53 wild-type disease who are candidates for aggressive induction. In the recurrent setting, single-agent bortezomib and single-agent lenalidomide are being removed, and lenalidomide plus rituximab is being added.

The key evidence discussion centered on TRIANGLE. The trial challenged the older transplant-centered pathway structure by showing that an ibrutinib-containing intensive regimen without planned autologous stem-cell transplant performed favorably compared with standard immunochemotherapy plus transplant. For pathway purposes, the panel focused on the induction strategy. The trial included maintenance therapy, but ibrutinib maintenance was considered out of scope for pathway evaluation.

The panel also recognized that first-line TP53-mutated mantle cell lymphoma should be considered out of scope for these standard pathway scenarios. This is a clinical accuracy issue rather than a utilization-management nuance. Standard intensive regimens are not the right comparator framework for TP53-mutated disease. The second-line changes were similarly pragmatic. Single-agent bortezomib and single-agent lenalidomide no longer reflect the current preferred treatment paradigm, while lenalidomide plus rituximab better aligns with contemporary practice.

CLL/SLL

What changed: Ibrutinib remains in the workbook, but only as appropriate for continuation in patients already receiving and tolerating treatment. The intended workbook note is: "Appropriate for continuation only in those already receiving and tolerating treatment."

The reason is not that ibrutinib has no clinical activity. The issue is that the treatment landscape has moved toward better-tolerated covalent BTK inhibitors and fixed-duration venetoclax-based combinations. For patients already doing well on ibrutinib, continuation can be reasonable. For new starts, the pathway should generally signal the preferred use of alternatives with more favorable tolerability or fixed-duration treatment characteristics.

The panel also discussed operational issues related to incomplete capture of oral agents. Some apparent single-agent antibody requests may actually represent combination treatment in which the oral component is not visible in the same workflow. This remains an important configuration and data-capture issue.

Multiple myeloma

What changed: Single-agent teclistamab is being added to the second-line myeloma pathway once approved for that setting, alongside teclistamab plus daratumumab, which had been added previously based on MajesTEC-3.

MajesTEC-9 was the key study. It compared teclistamab monotherapy with investigator's choice of PVD or Kd in relapsed or refractory multiple myeloma after one to three prior lines of therapy. The trial showed a large progression-free survival benefit, higher complete response or better rates, and an overall survival advantage at interim analysis. The panel viewed the study as highly relevant to contemporary practice because many patients now relapse after frontline daratumumab-containing therapy.

The discussion also recognized practical access differences between bispecific antibodies and CAR-T therapy. Most participating practices do not have on-site CAR-T capability, whereas bispecific therapy may be more directly implementable in many community oncology settings, provided the practice has the infrastructure to manage cytokine release syndrome risk, infection risk, and monitoring requirements.

Metastatic breast cancer

What changed: For metastatic triple-negative breast cancer, the TNBC pathway scope is being narrowed from first, second, and third lines to first and second lines. Single-agent datopotamab deruxtecan and single-agent sacituzumab govitecan are being added for first- and second-line stage IV or recurrent TNBC when immunotherapy is not appropriate. Sacituzumab govitecan plus pembrolizumab is being added for first-line stage IV or recurrent TNBC with PD-L1 CPS ≥ 10 . Third-line TNBC pathways are being removed from program scope.

The two ADC monotherapy trials were TROPION-Breast02 and ASCENT-03. TROPION-Breast02 evaluated datopotamab deruxtecan versus chemotherapy in previously untreated locally recurrent inoperable or metastatic TNBC for patients who were not candidates for immunotherapy. Datopotamab deruxtecan improved both progression-free survival and overall survival compared with chemotherapy and met criteria for ESMO-MCBS grade 4. ASCENT-03 evaluated sacituzumab govitecan versus chemotherapy in previously untreated metastatic TNBC for patients who were not candidates for PD-1/PD-L1 inhibitors. Sacituzumab govitecan improved progression-free survival, although overall survival interpretation was complicated by protocol crossover. The ESMO-MCBS score discussed for ASCENT-03 was grade 3.

The panel concluded that it would be difficult to add one ADC and not the other. The treatments have different toxicity profiles, and those differences should support

individualized clinical selection. The pathway should not imply that these ADCs should routinely be sequenced one after the other, however. The revised pathway language should state that sacituzumab and datopotamab may be used in only one line of therapy. For provider enablement and portal training, this should be more than a public workbook footnote if configuration allows. Second-line requests should ideally include an attestation that the patient has not already received one of these ADCs in the first-line setting.

The panel also added sacituzumab govitecan plus pembrolizumab for first-line TNBC with CPS ≥ 10 based on ASCENT-04. The ESMO-MCBS v2.0 form 2b score discussed for this regimen was grade 3. The panel recognized that overall survival and quality-of-life data were still immature, that PFS2 was exploratory, and that first-line use of sacituzumab govitecan may remove the option of later sacituzumab. Even so, the regimen is clinically compelling, FDA-approved, and likely to be incorporated into practice widely.

Prostate cancer

What changed: The PROTEUS perioperative regimen is not being added at this time. A post-prostatectomy workbook footnote will clarify that ADT may be used with or without radiotherapy as clinically appropriate. The panel did not restrict first-line metastatic scenarios to HRR-negative disease and did not expand pathway scope to include high-risk non-metastatic castration-resistant prostate cancer.

The PROTEUS trial evaluated perioperative ADT plus apalutamide versus perioperative ADT plus placebo for high-risk localized or locally advanced prostate cancer undergoing radical prostatectomy. The panel did not view the data as sufficient to add a new competing perioperative pathway category. Concerns included immature overall survival data, uncertainty around the metastasis-free survival definition, and the fact that both arms included perioperative ADT, which does not cleanly reflect the current surgical standard for many patients.

The panel also avoided adding biomarker-specific complexity to the first-line metastatic pathway. Although HRR status matters in prostate cancer, the relevant pathway options were not all developed exclusively in HRR-negative populations. Adding HRR-negative restrictions would likely increase configuration burden without improving the practical pathway framework. Similarly, high-risk non-metastatic castration-resistant disease was viewed as a niche scenario, often managed in urology settings, with challenging oral-agent data capture and no clear pathway-preferred option.

Bladder cancer

What changed: The NMIBC adjuvant clinical scenario will be clarified as applying to low- and intermediate-risk non-muscle invasive bladder cancer. High-risk NMIBC is not being added to pathway scope.

This change is mainly about clinical accuracy. The existing wording was too broad and could be read as applying to all stage 0, stage I, or recurrent NMIBC. The panel agreed that risk stratification matters and that the pathway should not imply that high-risk NMIBC is in scope.

KEYNOTE-B15/EV-304 further supports the evolving perioperative role of enfortumab vedotin plus pembrolizumab in muscle-invasive disease, but it did not require a Q3 pathway change since the regimen is already on pathway. POTOMAC, evaluating durvalumab plus BCG in high-risk NMIBC, was not added because of cost, lack of demonstrated overall survival or quality-

of-life benefit, open-label design concerns, and limited relevance to current pathway scope. IMvigor011 was also discussed and viewed as important for ctDNA-guided adjuvant therapy research, but not ready for pathway incorporation given the active-comparator issue, existing nivolumab pathway positioning, operational complexity, and a rapidly evolving perioperative treatment landscape.

Ovarian cancer

What changed: Pembrolizumab plus weekly paclitaxel, with or without bevacizumab, is being added as initial therapy for platinum-resistant metastatic or recurrent ovarian cancer in the appropriate PD-L1-positive context of CPS greater than or equal to 1. Relacorilant plus nab-paclitaxel is also being added as initial therapy for platinum-resistant metastatic or recurrent disease. Ovarian histology scope will be clarified to include high-grade serous carcinoma, grade 2/3 endometrioid carcinoma, clear cell carcinoma, and carcinosarcoma. Low-grade serous and mucinous histologies are excluded from the pathway denominator. Doxil plus bevacizumab is not being added as a new pathway regimen.

KEYNOTE-B96 evaluated pembrolizumab versus placebo with weekly paclitaxel, with optional bevacizumab, in platinum-resistant recurrent ovarian cancer. The regimen produced a clinically meaningful overall survival benefit in the PD-L1-positive population, despite only modest progression-free survival improvement. The ESMO-MCBS grade discussed for this regimen was grade 3. The panel recognized the added toxicity, cost, and treatment complexity, but also recognized the high unmet need in platinum-resistant ovarian cancer and the importance of an overall survival signal in this setting.

ROSELLA evaluated relacorilant plus albumin-bound paclitaxel versus albumin-bound paclitaxel alone in platinum-resistant ovarian cancer after up to three prior lines of therapy and prior bevacizumab. The regimen improved progression-free survival and showed a clinically meaningful overall survival benefit. It was described as ESMO-MCBS grade 4, consistent with substantial clinical benefit.

The panel discussed the scope of pathways for platinum-resistant metastatic/recurrent ovarian cancer, confirming that it includes first through third lines of therapy. As such, fourth and later lines should not be explicitly counted as off pathway (since they are outside program scope), but it is noteworthy that late lines of therapy are less evidence-based. It is acknowledged that Doxil plus bevacizumab may still be reasonable for selected patients, including those with baseline neuropathy, taxane intolerance, prior significant taxane toxicity, or a strong preference to avoid alopecia. This regimen is not considered as a pathway option because the available comparative evidence did not show superiority over paclitaxel plus bevacizumab for the typical patient. Noteworthy also is that KEYNOTE-B96 and ROSELLA now added new evidence-supported choices in this setting where there has been unmet clinical need.

Colorectal cancer

What changed: Encorafenib plus cetuximab with FOLFIRI is being added for first-line stage IV or recurrent BRAF V600E mutation-positive colorectal cancer. CapeOX plus atezolizumab is being added administratively for adjuvant stage III colon cancer limited to MSI-H or dMMR disease.

The BREAKWATER Cohort 3 discussion focused on whether the pathway should include an irinotecan-based encorafenib/cetuximab option alongside the existing oxaliplatin-based approach. The panel agreed that FOLFIRI plus encorafenib/cetuximab is important for patients who are not good candidates for oxaliplatin, particularly those with baseline neuropathy. The toxicity profile did not create a major concern given the demonstrated benefit and the clinical need for an oxaliplatin-sparing option.

The CapeOX plus atezolizumab update was handled administratively because it was consistent with NCCN positioning and did not require a separate panel discussion. The disease context is narrow: adjuvant stage III colon cancer with MSI-H or dMMR disease.

Cross-cutting implementation themes

Several Q3 decisions were not just about whether a regimen works. They were about whether the pathway structure can accurately represent the intended clinical use. The recurring themes were scope, sequencing, biomarker capture, oral-agent visibility, and line-of-therapy clarity.

- Scope matters. TNBC and HR-positive/HER2-negative metastatic breast cancer third-line pathways are being removed from scope. High-risk NMIBC remains out of scope. Later-line ovarian requests need clear denominator handling.
- Sequencing matters. Sacituzumab and datopotamab should not be used as routine sequential ADC therapy without supporting evidence.
- Biomarker capture matters. TP53 status in MCL, PD-L1 status in TNBC and ovarian cancer, HRR status in prostate cancer, and MSI-H/dMMR status in colon cancer all illustrate that a pathway can only be as accurate as the clinical data captured.

Practical bottom line

The largest clinical additions were in metastatic TNBC, platinum-resistant ovarian cancer, relapsed/refractory multiple myeloma, mantle cell lymphoma, and BRAF V600E-mutant colorectal cancer. The most important scope clarifications were removal of third-line metastatic breast cancer pathways, specifying the scope of NMIBC includes only low- and intermediate-risk disease, and clearer line-of-therapy framing for platinum-resistant ovarian cancer.