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CA 125 KELIM and Chemotherapy Response Score as Complementary Tools for Optimizing Bevacizumab Use in Advanced Ovarian Cancer

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ABSTRACT

Advanced epithelial ovarian cancer remains challenging to treat. Bevacizumab added to first-line therapy provides a modest progression-free survival benefit, but its overall benefit is concentrated in selected high-risk patients. Traditional clinical factors do not fully capture underlying tumor biology. This creates a need for biomarkers that better reflect treatment response. This review examines the CA-125 elimination rate constant, KELIM, and Chemotherapy Response Score as complementary tools to guide bevacizumab use in advanced ovarian cancer. KELIM is an early, dynamic marker of intrinsic chemosensitivity. Phase III evidence suggests that patients with low or unfavorable KELIM are more likely to benefit from bevacizumab, whereas those with favorable KELIM derive less benefit. CRS is a postoperative, tissue-based score that is strongly prognostic. CRS1 or CRS2 indicates higher-risk disease, but CRS is not yet a formal predictor of bevacizumab benefit. Together, KELIM and CRS may improve patient selection for anti-angiogenic therapy. Prospective validation and integration with additional molecular markers remain needed.

Introduction

Despite advances in surgery and systemic therapy, advanced epithelial ovarian cancer often relapses and responds variably to treatment. Adding bevacizumab, an anti-VEGF monoclonal antibody, to first-line therapy modestly improves progression-free survival [1]. Overall survival benefit is mostly seen in specific high-risk groups [1]. Identifying which patients will benefit from bevacizumab is still a key challenge. Traditional clinical factors like stage, postoperative residual disease, and performance status only tell part of the story, they don't capture the underlying tumor biology [2,3]. Because of this, the spotlight is now on biomarkers that better reflect how a tumor responds to treatment. Newer tools like the CA 125 elimination rate constant (KELIM) and the Chemotherapy Response Score (CRS) are giving doctors a clearer, more personalized picture of how a patient's tumor is likely to respond to treatment [4]. By using these markers,

doctors can make more informed decisions and tailor therapies to each individual, rather than relying on a one-size-fits-all approach [4]. This review analyzes the biological basis, clinical evidence, and possible combined role of KELIM and CRS in guiding bevacizumab use.

Biological Rationale: Chemosensitivity and Angiogenesis

Bevacizumab works by blocking the formation of new blood vessels that tumors need to grow, rather than making chemotherapy itself more powerful. Interestingly, even when tumors don't respond well to platinum-based chemotherapy, they may still rely on these blood vessel pathways for survival [1,2]. That's why blocking VEGF with bevacizumab can be especially effective in these resistant tumors [2,3]. Conversely, highly chemosensitive tumors may derive limited incremental benefit from bevacizumab, as chemotherapy alone already achieves successful disease control [5]. Thus, biomarkers that quantify chemosensitivity provide a biological basis for guiding the use of bevacizumab.

CA 125 KELIM: A Dynamic Marker of Tumor Chemosensitivity

KELIM is a calculated value based on how a patient's CA 125 levels change over the first 100 days of platinum-based chemotherapy. In simple terms, it shows how fast CA 125 falls and gives doctors an early indication about how sensitive the cancer is to chemotherapy [4]. If the KELIM is high (kelim > 1), it usually means the tumor is responding well; if it's low, the cancer is likely more resistant [4]. Major phase III trials, [5,6] show KELIM predicts bevacizumab benefit. In the ICON 7 trial, [6] patients with unfavorable KELIM and high-risk disease (stage IV or suboptimally debulked stage III) lived longer with bevacizumab. Patients with favorable KELIM did not benefit from improved overall survival. The GOG 0218 trial [5] confirmed that bevacizumab improves progression-free survival in patients with unfavorable KELIM, but not in those with favorable KELIM. These results show that bevacizumab is most useful for patients with low KELIM and poor intrinsic chemosensitivity [5-7].

Chemotherapy Response Score (CRS)

Definition and Clinical Significance

CRS is a simple three-level scoring system that pathologists use to grade how much a tumor has responded to chemotherapy. After neoadjuvant chemotherapy and interval surgery, they look at the tissue (usually from the omentum, sometimes the adnexa) and assign a score: CRS1 means the tumor barely responded, CRS2 shows a partial response, and CRS3 means the cancer responded almost completely [8]. This score isn't just a number; it's a powerful predictor of outcomes. Patients with CRS3 usually have much longer progression-free and overall survival compared to those with CRS1 or CRS2 [8].

CRS and Bevacizumab: Indirect Evidence

Unlike KELIM, CRS hasn't been officially proven to predict who will benefit from bevacizumab. Still, looking at studies after the fact gives us some interesting clues. In patients who don't get bevacizumab, a high CRS score (CRS3) clearly signals a much better chance at long-term survival [9]. But for patients who do receive bevacizumab maintenance, the survival gap between high and low CRS scores seems to shrink or even disappear [9]. This suggests that bevacizumab might help counteract the disadvantage for patients whose tumors didn't respond well to chemotherapy, rather than CRS being a direct guide for bevacizumab use.

Integrating KELIM and CRS: A Complementary Framework

KELIM and CRS give us different snapshots of how a tumor responds to chemotherapy, using different methods and timing. KELIM is an early, blood-based marker that tracks changes during treatment, while CRS is a tissue-based score evaluated after surgery following chemotherapy. Both help flag patients with poor chemosensitivity; the group most likely to benefit from adding bevacizumab. When a patient's KELIM score is low, research shows they're more likely to benefit from bevacizumab [5]. A low CRS score (CRS1 or CRS2) signals a higher-risk cancer, [8,9] where bevacizumab may be especially important, even though CRS isn't a formal predictor. Together, these tools give doctors reassurance and clarity when deciding on bevacizumab, especially if one test isn't available or the results are unclear. This means patients are more likely to get the right treatment for their specific situation.

Limitations and Future Directions

Several limitations warrant consideration. KELIM requires serial CA 125 measurements and specialized modeling, limiting its broad adoption. CRS is applicable only to patients undergoing NACT and interval debulking surgery [8]. Most data supporting the use of biomarker guided bevacizumab are retrospective [5,6]. Prospective validation of biomarker driven treatment strategies, integration with molecular markers (e.g., HRD status), and evaluation in the era of combined anti angiogenic and PARP inhibitor maintenance are needed.

Conclusion

CA 125 KELIM and CRS each bring something valuable to the table when figuring out the best use of bevacizumab for ovarian cancer. If a patient's KELIM score is low, studies show they're more likely to benefit from bevacizumab. A low CRS (CRS1 or CRS2) points to a higher-risk type of cancer, where bevacizumab might be especially important, even though CRS isn't yet a formal predictor. Used together, these tools help doctors feel more confident in their decisions, especially if one marker isn't available or gives an unclear result. This means more patients can get the right treatment for their specific situation, rather than relying solely on traditional clinical features.

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