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ABSTRACT & COMMENTARY

Second-line Docetaxel Improves Survival and Symptom Control in Advanced Esophagogastric Cancer

By Gary R. Shapiro, MD

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Dr. Shapiro reports no financial relationships relevant to this field of study.

SYNOPSIS: Patients with progressive advanced esophagogastric adenocarcinoma treated with docetaxel in addition to active symptom control (ASC) survived 44% longer than those who received ASC alone. In addition to a 5.2 vs 3.6 months increase in overall survival, improved symptom control was observed in the patients receiving docetaxel.

SOURCE: Ford HE, et al. Docetaxel versus active symptom control for refractory oesophagogastric adenocarcinoma (COUGAR-02): An open-label, phase 3 randomized controlled trial. *Lancet Oncol* 2014;15:78-86.

This Phase 3 randomized trial compared salvage chemotherapy with docetaxel (75 mg/m^2 every 3 weeks for up to six cycles) plus active symptom control (ASC) with ASC alone in patients with locally advanced (12.5%) or metastatic (87.5%) adenocarcinoma of the esophagus (20%), esophagogastric junction (35%), or stomach (45%) that had progressed on or within 6 months of treatment with a platinum-fluoropyrimidine chemotherapy combination (which could have been given as adjuvant or neoadjuvant therapy, or for advanced disease). This multicenter study (the COUGAR-02 trial) was conducted in the United Kingdom, and included only patients who had an Eastern Cooperative Oncology Group performance score of 0-2 and satisfactory hematological, renal, and hepatic function. Health-related quality of life (HRQoL) was assessed in all participants using standard (QLQ-C30 and EORTC QLQ-STO22) questionnaires at baseline and at periodic intervals throughout the course of therapy.

The COUGAR-02 study showed that second-line docetaxel improved median overall survival compared with ASC alone — 5.2 months vs 3.6 months. Overall survival in the docetaxel group was 82% at 2 months and 39% at 6 months, compared to 84% and 23% in the ASC alone group. Two-thirds of the 84 patients who received docetaxel were assessable for response, with the best response being partial in 4 (7%) and stable diseases in 24 (43%).

A median of three docetaxel treatment cycles was

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administered, with only 23% of patients in the docetaxel group completing all six cycles and 20% only one cycle. The main reasons for stopping docetaxel early were progression of disease (40%), unacceptable toxicity (31%), and death from cancer (15%). None of these deaths was attributed to chemotherapy. As one would expect, docetaxel was associated with higher incidence of grade 3-4 neutropenia (15% vs 0) and febrile neutropenia (7% vs 0). Patients receiving docetaxel reported less general pain ($P = 0.0008$), less nausea and vomiting ($P = 0.02$), and less constipation ($P = 0.02$) than those who received ASC alone. Disease-specific HRQoL measures also showed benefits for docetaxel in reducing dysphagia ($P = 0.02$) and abdominal pain ($P = 0.01$). The mean overall quality-adjusted life weeks was 12.1 weeks for the docetaxel/ASC group and 9.3 weeks for the ASC alone control group.

COMMENTARY

Previous studies[1,2] have suggested that second-line treatment may extend survival in patients with advanced esophagogastric adenocarcinoma, but this is the first well-designed, randomized, controlled trial that includes rigorous quality-of-life assessments, and it is for this that the COUGAR-02 is most noteworthy. Although COUGAR-02 conclusively shows that those treated with docetaxel in addition to ASC survived 44% longer than those who received ASC alone, someone who takes the time to do the math may reasonably question whether an additional "statistically significant" 1.6 months of life is all that meaningful. However, there is no questioning the benefit of improved symptom control and quality of life that those who received docetaxel enjoyed compared to those who did not. Active symptom management is important, but even the best supportive care has its limitations.

Of course, palliative chemotherapy is not for everybody. The COUGAR-02 investigators should be congratulated for including "real world" older (23%) and symptomatic ECOG performance status 2 (15%) patients in their trial, but many esophagogastric cancer patients spend significantly more than half of their waking hours in bed or in a chair (ECOG performance status 3 or 4) and are older than the 65 years median age of the COUGAR-02 patients. Indeed, subgroup analysis showed that performance status (ECOG 0 better than ECOG 1 or 2; $P = 0.001$) and disease status (locally advanced better than metastatic; $P = 0.006$) were predictors of overall survival.

Paclitaxel and irinotecan have also shown activity as second-line chemotherapy for advanced esophagogastric adenocarcinoma, and there is certainly ample room for new regimens.[3,4] For now, the COUGAR-02 study provides the most compelling reason to date for oncologists and patients to consider docetaxel the standard of care for those who are reasonably fit following first-line treatment with a platinum-fluoropyrimidine chemotherapy combination. ■

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ABSTRACT & COMMENTARY

Bendamustine-Bortezomib-Dexamethasone for Relapsed Myeloma

By William B. Ershler, MD, Editor

SYNOPSIS: In a Phase 2 trial, Ludwig and colleagues present data on 79 patients with relapsed or refractory myeloma who were treated with bendamustine in combination with bortezomib and dexamethasone. The combination was well tolerated and resulted in a 75% response rate (including those with "minor" response). Responses occurred early (first noted at approximately 1 month) and progression-free survival was 9.7 months. Responses occurred in patients with adverse cytogenetics, higher stage, and prior exposure to bortezomib and/or lenalidomide.

SOURCE: Ludwig H, et al. Bendamustine-bortezomib-dexamethasone is an active and well-tolerated regimen in patients with relapsed or refractory multiple myeloma. *Blood* 2014;123:985-991.

Recent advances in myeloma therapy have resulted in significant improvements in response rates and overall survival for patients with multiple myeloma. Yet the great majority of patients relapse and the optimal second-line therapy remains to be established. Typically second treatments are configured based on a number of patient-related factors as well as prior drug exposure. In this regard, bendamustine represents an attractive component for a second-line regimen. The bendamustine molecule is composed of three structural elements: a mechlorethamine (nitrogen mustard) group, a benzimidazole ring, and a butyric acid side chain. The mechlorethamine (nitrogen mustard) group is similar to other alkylators like cyclophosphamide and chlorambucil. The benzimidazole ring, which replaces the benzene ring present in chlorambucil, is unique and is similar in structure to some purine analogs such as 2-chlorodeoxyadenosine. This observation has led some to hypothesize that bendamustine may have purine analog activity as well. Laboratory studies indicate unique properties of this drug, especially when compared with other alkylators. DNA breaks induced by bendamustine are significantly greater in number than those produced by cyclophosphamide or carmustine and are more durable than those associated with melphalan, cyclophosphamide, or carmustine.[1,2] Evidence in human breast carcinoma cells shows that bendamustine-induced DNA breaks are more difficult to repair than those induced by carmustine or cyclophosphamide, and that repair of DNA damage is slower than with other alkylating agents. Bendamustine lacks cross-reactivity with many other cancer drugs, including melphalan and several other cytotoxic drugs,[3] and has been shown to overcome resistance to melphalan as well as dexamethasone in myeloma cell lines.[4,5]

The current Phase 2 trial was conducted throughout Austria and the Czech Republic. Bendamustine with bortezomib and dexamethasone was evaluated in 79 patients with relapsed/refractory multiple myeloma. The median age was 64 years, and all but four of the patients were ECOG performance status 0 or 1. Enrolled patients had a median of two prior treatment lines (range, 1 to 6 lines). Patients were given bendamustine 70 mg/m^2 days 1 and 4; bortezomib 1.3 mg/m^2 intravenously days 1, 4, 8, and 11; and dexamethasone 20 mg days 1, 4, 8, and 11 once every 28 days for up to eight cycles. Primary endpoint was overall response rate (ORR). Secondary endpoints were progression-free survival (PFS), overall survival, time to response, and toxicity. Myeloma response was assessed according to the International Uniform Response Criteria for Multiple Myeloma[6] with the addition of the minor response category.[7] The ORR was 60.8%, and when minor responses were included, 75.9%. Median time to response was 31 days. ORR rate was similar in patients previously exposed to bortezomib, lenalidomide, and bortezomib plus lenalidomide. PFS was 9.7 and OS was 25.6 months. Multivariate analysis showed high lactate dehydrogenase, three or more prior treatment lines, and low platelet count independently correlated with short survival. Grade 3/4 thrombocytopenia was noted in 38%, and grade 3/4/5 infections were noted in 23%. Grade 1 or 2 polyneuropathy increased from 19% at baseline to 52% at cycle 8, and grade 4 from 0% to 7%.

COMMENTARY

With the introduction of novel agents such as lenalidomide and bortezomib, prior alkylating agent exposure is less commonly encountered in patients with relapsed myeloma, particularly for those who were not treated with stem cell therapy. Bendamustine had previously been tested as single-agent (with prednisone) initial therapy and in combination with either lenalidomide or bortezomib in patients with relapsed or refractory myeloma. In this larger Phase 2 trial, bendamustine with bortezomib and dexamethasone resulted in an overall response rate (including minor responses) of > 75% with PFS of 9.7 months and OS of 25.6 months. Of particular interest was the relatively short time to response (31 days) and to best response (111 days), a feature that may well correlate with improved quality of life — although this was not measured in this trial. It is notable that comparable short time to response was also apparent when bendamustine was combined with lenalidomide and corticosteroids.[8,9]

Thus, bendamustine-bortezomib-dexamethasone is active and reasonably well tolerated in patients with relapsed/refractory myeloma. The patients enrolled in the current study, albeit with relapsed or refractory myeloma, were younger (median age 64 years) and healthier (ECOG PS 0-1 in 94%) than typically observed in most myeloma clinics. Thus, it remains to be seen whether this combination will be suitable for older patients, particularly those with existing comorbidities or significant functional impairment. In this regard, bendamustine in combination with carfilzomib might be an interesting comparator, in light of its favorable toxicity profile.[10] ■

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ABSTRACT & COMMENTARY

Strategy to Overcome Rituximab Resistance in Patients with Indolent Lymphoma

By William B. Ershler, MD, Editor

SYNOPSIS: In a Phase 2 study, Ahmadi and colleagues demonstrate reasonably high response rates in rituximab-resistant indolent lymphoma patients sequentially treated with lenalidomide/dexamethasone (Part 1; 2 monthly cycles) followed by lenalidomide/dexamethasone + weekly rituximab (Part 2; 3 monthly cycles). Of the 24 evaluable patients, the overall response rate was 29% and 58% in Parts 1 and 2, respectively. The data suggest that lenalidomide treatment may result in a return of rituximab sensitivity in patients previously known to be resistant.

SOURCE: Ahmadi T, et al. Combined lenalidomide, low-dose dexamethasone, and rituximab achieves durable responses in rituximab-resistant indolent and mantle cell lymphomas. *Cancer* 2014;120:222-228.

Rituximab is widely used both as a single agent, and in combination with chemotherapy for treatment of B-cell non-Hodgkin lymphomas, and has been shown to improve outcomes.[1,2] However, unfortunately, many patients develop resistance to rituximab, and this is associated with worse outcomes including reduced survival. A previous study by Abdollahi and colleagues examined patients with follicular lymphoma who developed resistance to rituximab and demonstrated a significant decrease in 5-year overall survival (58%) when compared to all patients with follicular lymphoma.[3]

Lenalidomide is an immunomodulatory drug shown to have benefit in the treatment of relapsed and refractory B-cell lymphomas when used as a single agent.[4,5] It has been suggested that lenalidomide increases antibody-dependent, cell-mediated cytotoxicity and thus decreases tumor-induced resistance.[6] Such an immunologic effect may potentially enhance the antitumor activity of rituximab.

Ahmadi and colleagues conducted a single-center, prospective, Phase 2 clinical trial to investigate the efficacy of lenalidomide combined with rituximab in patients with previously treated, rituximab-refractory or resistant, indolent B-cell or mantle cell lymphoma. Inclusion criteria were as follows: adults (aged ≥ 18 years) with histologically confirmed progressive CD20 antigen-expressing follicular (grades 1, 2, and 3a), marginal zone, small lymphocytic, lymphoplasmacytic, or mantle cell lymphomas, life expectancy > 3 months, and at least one measurable lesion that was ≥ 2 cm.

The protocol was divided into two parts. Part 1 consisted of two 28-day treatment cycles during which all patients received lenalidomide 10 mg PO daily. Dexamethasone was added to the treatment regimen based on clinical experience suggesting that it was beneficial in reducing the side effects of lenalidomide, particularly rash, as well as the previously described synergy between corticosteroids and lenalidomide.[7] All patients received dexamethasone 8 mg weekly. Response evaluation, including CT or PET/CT, was performed at the end of the two treatment cycles (Part 1 response). All patients, regardless of Part 1 response, continued on to Part 2, which included three 28-day treatment cycles (cycles 3 through 5). During these 3 cycles, lenalidomide and dexamethasone were continued and all patients received rituximab 375 mg/m^2 weekly. Response evaluation was reassessed at the end of cycle 5. Patients with stable disease or a partial response continued treatment with lenalidomide with or without dexamethasone until they developed disease progression or withdrew from the study. Restaging evaluations were done at 12, 18, and 24 months after study enrollment and then annually for a maximum of 5 years. The primary endpoint was the overall response rate (ORR) after cycle 5 (Part 2 response). Secondary endpoints included ORR after cycle 2 (Part 1 response), progression-free survival (PFS), response duration (RD), time to progression (TTP), and toxicity evaluation.

Twenty-seven patients with follicular (n = 18), mantle cell (n = 5), small lymphocytic (n = 3), and marginal zone (n = 1) lymphomas were enrolled between July 2008 and May 2010. The median age at enrollment was 60 years (range: 35-85) and time from diagnosis was 6.77 years (range: 0.89-26.12 years).

Three of the 27 enrolled patients discontinued treatment due to adverse events prior to cycle 3. Twenty-four patients received rituximab during cycle 3 and were evaluable for both part 1 and part 2 responses. For these patients, the ORR after part 1 was 29% (four patients had a complete response [CR] or CR unconfirmed [CRu], and three patients had a partial response [PR]). The ORR after part 2 was 58% (eight patients had a CR and six had a PR). The ORR was 53% for patients with follicular lymphoma (8/15), 60% for mantle cell lymphoma (3/5), 67% for small lymphocytic lymphoma (2/3), and 100% for marginal zone lymphoma (1/1). Seventy-five percent of patients (19/24) continued to receive treatment with lenalidomide and dexamethasone after cycle 5. The median follow-up for all enrolled patients (n = 27) was 12.2 months (range: 0.9-52.7 months) and the median PFS was 23.7 months.

Four patients discontinued therapy due to adverse events thought to be treatment related. Of these, three discontinued treatment during part 1 (myocarditis, rash, thrombocytopenia), and one discontinued treatment after the part 2 response assessment (secondary malignancy). The most common grade 3 and 4 toxicities included neutropenia (30%), leukopenia (15%), hypokalemia (15%), anemia (7%), hypophosphatemia (7%), and thrombocytopenia (7%).

COMMENTARY

In summary, treatment with lenalidomide, low-dose dexamethasone, and rituximab was shown to be effective in patients with rituximab-refractory or resistant indolent B-cell or mantle cell lymphoma. This combination, administered at different doses or on different schedules, has previously been shown to be an effective regimen for both indolent and aggressive lymphoma variants, either as initial treatment or for relapsed or refractory disease. However, what makes this trial unique is that each of the enrolled patients had demonstrated prior rituximab resistance. The current data suggest that prior and concurrent lenalidomide is effective in at least partially overcoming rituximab resistance, thereby explaining the delta in observed responses when comparing rates at the end of Part 2 with those after completion of Part 1. However, the study was not designed to prove this conclusively and it might be reasonably argued that the increment in response rates during Part 2 reflected a cumulative, delayed effect of lenalidomide alone. To address this, a prospective randomized trial of lenalidomide/dexamethasone ± late cycle rituximab would be most instructive. ■

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ABSTRACT & COMMENTARY

Toward More Effective Neoadjuvant Breast Cancer Therapy

By William B. Ershler, MD, Editor

SYNOPSIS: In a Phase 3, randomized clinical trial of primary systemic therapy for patients with early, locally advanced breast cancer, the addition of capecitabine to each of six 3-weekly cycles of epirubicin-docetaxel resulted in a 1.64 fold increase in the possibility of primary tumor pathologic complete response. Small tumor size, hormone receptor negative disease, and high-grade cellular features were predictors of the greatest benefit of neoadjuvant treatment.

SOURCE: Steger GG, et al, on behalf of the Austrian Breast and Colorectal Study Group (ABCSG). Epirubicin and docetaxel with or without capecitabine as neoadjuvant treatment for early breast cancer: Final results of a randomized phase III study (ABSG-24). *Ann Oncol* 2014;25:366-371.

Neoadjuvant chemotherapy is now considered treatment of choice for locally advanced, newly diagnosed breast cancer, particularly when patients are not candidates for immediate breast-conserving surgery (BCS).[1] Such is based on observations that primary systemic therapy (PST) downstages the primary tumor and lymph node metastases[2,3] and increases opportunities for BCS. PST also provides the opportunity to assess chemosensitivity in vivo and to apply therapy early in a disease with a high distant failure rate. The Austrian Breast and Colorectal Study Group (ABCSG) previously demonstrated that duration of therapy impacts pathologic complete response (pCR) rate,[4] and additional analyses have shown a correlation between pCR and extended disease-

free survival (DFS) and overall survival (OS).[5] This supports the conclusion that pCR of the primary tumor is a surrogate marker for eradication of micrometastases and improved survival. Published data show pCR rates of approximately 20% with anthracycline-taxane regimens.[4,6] The question remains whether the addition of a third drug would improve this response without unacceptable toxicity. For this, capecitabine (C) seemed the logical choice as it has a favorable toxicity profile, is effective as monotherapy, and has been shown to improve response rates in patients with metastatic breast cancer when used with taxanes.[7]

In this light, the ABCSG conducted the current Phase 3 trial to compare pCR rates after PST of breast cancer following neoadjuvant epirubicin-docetaxel (ED) ± C, and evaluated the addition of trastuzumab in HER2-positive tumors.

Patients with invasive breast cancer (except T4d) were randomly assigned to receive six 3-weekly cycles of ED (both 75 mg/m^2) ± C (1000 mg/m^2, twice daily, days 1–14). Patients with HER2-positive disease were further randomized to receive trastuzumab (8 mg/kg, then 6 mg/kg every 3 weeks) or not. The study primary endpoint was tumor pCR rate at the time of surgery.

A total of 536 patients were randomized to ED (n = 266) or EDC (n = 270); 93 patients were further randomized to trastuzumab (n = 44) or not (n = 49). pCR rate was significantly increased with EDC (23.0% vs 15.4% ED; $P = 0.027$) and nonsignificantly further increased with trastuzumab (38.6% EDC vs 26.5% ED, $P = 0.212$). Rates of axillary node involvement at surgery and breast conservation were improved with EDC vs ED but not significantly; the addition of trastuzumab had no further impact. Hormone receptor status, tumor size, grade, and the addition of capecitabine were independent prognostic factors for pCR (all $P \leq 0.035$).

COMMENTARY

These findings (an improved pCR rate from 15.4% to 23.0%) show that the integration of capecitabine into a neoadjuvant taxane-/anthracycline-based regimen is an effective treatment option for locally advanced breast cancer. Although the benefit observed is what might be expected from the incremental advantage of adding capecitabine to regimens in the treatment of metastatic breast cancer, two prior studies had indicated no added benefit in the neoadjuvant setting.[8,9] However, as the authors point out, in both trials capecitabine was used at lower dose and only for four cycles. It is notable that in addition to capecitabine use, the hormone receptor status, tumor stage, and grade were independent prognostic factors for pCR. Hormone receptor-negative disease and undifferentiated (G3) tumors were associated with a significant increased chance of pCR after treatment with ED or EDC. In particular, triple-negative tumors (most of which are high grade) reached a pCR rate of 45.3% in this trial. Thus, further neoadjuvant studies might well focus on TNBC.

This was a large, carefully conducted multicenter prospective, randomized clinical trial and the findings are of value. U.S. oncologists are less familiar with the epirubicin-docetaxel regimen and the immediate applicability of the published report will more likely occur in Europe or elsewhere. However, it can be concluded that the integration of capecitabine into taxane/anthracycline-based neoadjuvant strategies is feasible, safe, and of demonstrable efficacy. The identification of greatest benefit in those with high-grade, triple-negative disease is of additional importance. ■

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ABSTRACT & COMMENTARY

Cancer-reducing Effect of OCPs in BRCA1/BRCA2 Carriers: Do They Work?

By Robert L. Coleman, MD

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Dr. Coleman reports no financial relationships relevant to this field of study.

This article originally appeared in the March 2014 issue of *OB/GYN Clinical Alert*.

SYNOPSIS: The association between oral contraceptive use and ovarian or breast cancer in BRCA1 or BRCA2 mutation carriers are qualitatively similar to associations reported in the general population. Oral contraceptive pill use is inversely associated with ovarian cancer risk. However, it is also associated with a modest, but not statistically significant, increased risk for breast cancer. The analysis was unable to provide conclusive recommendations as to their use as preventive measures given these and other unmeasured risks. However, oral contraceptive pills appear safe for contraception in this population.

SOURCE: Moorman PG, et al. Oral contraceptives and risk of ovarian cancer and breast cancer among high-risk women: A systematic review and meta-analysis. *J Clin Oncol* 2013;31:4188-4198.

Risks for ovarian and breast cancer are substantially elevated in women who carry germline mutations in BRCA1/2. The most effective method of cancer prevention is surgical resection; however, in those who wish to preserve fertility options, non-permanent prevention strategies are desired. Currently, non-invasive screening is unproven even in this high-risk cohort. Oral contraception pills (OCP) have been documented to reduce ovarian cancer risk in the general population and the magnitude of effect is related to the duration of use. The current study was conducted to analyze the known datasets of OCP use in high-risk women (i.e., carriers of BRCA1/2 or with a strong family history) for ovarian and breast cancer risk. The meta-analysis considered 6476 unique citations examining ovarian and breast cancer risk and settled on six addressing ovarian cancer risk and eight addressing breast cancer risk. Among germline mutation carriers combined, the meta-analysis demonstrated an inverse association between OCP use and ovarian cancer (odds ratio [OR], 0.58; 95% confidence interval [CI], 0.46-0.73) and a non-statistically significant association with breast cancer (OR, 1.21; 95% CI, 0.93-1.58). Findings were similar when examining BRCA1 and BRCA2 mutation carriers separately. The data were inadequate to perform a meta-analyses examining duration or timing of use. Additionally, there were four studies examining risk for ovarian cancer and three for breast cancer among women with a family history of ovarian or breast cancer. However, differences between studies precluded combining the data for meta-analyses, and no overall pattern could be discerned. The authors concluded that ever use of OCPs in women carrying a germline mutation in BRCA1 or BRCA2 was similar to that demonstrated in studies of population-risk patients. However, risk/benefit could not be directly addressed precluding a recommendation for their use for prevention of ovarian cancer.

COMMENTARY

"Oral contraceptive use had no significant effect on ovarian, breast cancer risk in BRCA1/2 carries" was the headline in a recent medical periodical highlighting this specific article. As can be appreciated, the sound bite is misleading, and although it gets one aspect correct (impact on breast cancer), it is stated with the intent to highlight the lack of protection by OCPs for ovarian cancer (false) and breast cancer (false) development in this high-risk group. While the authors clearly demonstrate an inverse protective effect of OCP use and ovarian cancer, the concern was not in protection of breast cancer but rather that OCP use would increase breast cancer risk, particularly in this patient cohort of individuals at substantially higher risk of breast cancer. Previous reports have raised concerns that OCP use may increase breast cancer risk in the general population.[1,2] The authors demonstrated an OR for breast cancer risk of > 1.0, but it was not statistically significant. Overall, this should be reassuring, yet, it was concluded that there was a "non-statistically significant" association of OCP use and the development of breast cancer.

This experience raises two take-home messages: first, headlines and sound bites may be very misleading and should be reproduced with caution; and second, data from observational studies and meta-analyses are hypothesis-generating and should be limited in their scope to these activities. Although, randomized controlled trials are the gold standard in assessing effect, such studies involving an intervention like OCPs are impractical. However, properly designed and monitored cohort studies, in this setting, can provide strong estimates of effect. Third, meta-analyses are tricky to perform properly, and heterogeneity in study design, patient cohorts, treatment or intervention used, follow-up, and confounders of the individual trials included in the exercise make it extremely difficult to assess questions of risk.[3] As was appreciated in this current study, the ratio of assessable trials filling the eligibility criteria was about 1:1000 in the reported literature. Finally, we are cautioned to accept even the author's conclusion based on the presented data. In this manuscript, the authors state "There is insufficient evidence to recommend oral contraceptive use as a chemoprevention strategy in high-risk women, if they otherwise would not be taking them for contraception." At face value this may be true, but the intent was not to diminish the effect seen in their use, but rather to provide a statement regarding the risks of OCP use (which they

could not assess due to trial heterogeneity in their sample set) and benefits (which they did evaluate in their sample set).[4] As is often the case, medical practice is governed by imperfect data and we are left to critically interpret the information before us; this should be done with caution. ■

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Continuing Education Questions

1. Which of the following is *true* about second-line docetaxel chemotherapy in patients with advanced esophagogastric adenocarcinoma?

a. Docetaxel increases overall survival but does not improve quality of life.
b. Docetaxel has no effect on survival but it improves quality of life.
c. Docetaxel improves both survival and quality of life.
d. None of the above

2. Which of the following pre-treatment characteristics was *not* associated with shortened survival for patients treated with bendamustine-bortezomib-dexamethasone in the Austrian-Czech Phase 2 trial.

a. High LDH
b. Adverse cytogenetics
c. Low platelet count
d. Three or more prior myeloma treatment regimens

3. The Phase 2 study of lenalidomide-dexamethasone-rituximab for patients with non-Hodgkin lymphoma (NHL) was unique because it:

a. included escalating doses of lenalidomide in late cycles.
b. enrolled only patients known to be resistant to rituximab.
c. compared response rates in patients with varying NHL histologies.
d. was the first to combine lenalidomide with rituximab for indolent histology NHL.

4. In the Austrian Breast and Colorectal Study Group trial, the primary endpoint was:

a. disease-free survival.
b. detection of positive axillary nodes at time of surgery.
c. tumor pCR at time of surgery.
d. tumor and axillary node pCR at the time of surgery.

5. Which of the following is *true* regarding the study of oral contraceptive pill use and cancer risk?

a. It is best described as a cohort study of BRCA1/2 women.
b. The patient population did not include patients with a strong family history of ovarian or breast cancer.
c. The association of OCP use and breast cancer was linear, but not statistically significant.
d. The statistic used to assess association was relative risk.

Pharmacology Watch and *Clinical Briefs* Available Online

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[IN FUTURE ISSUES] Exploring the use of temozolomide in patients with colorectal cancer