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INSIDE

Chemotherapy Offers Survival Benefit in Androgen-Independent Prostate Cancer

ABSTRACT & COMMENTARY

Synopsis: *In a trial that included androgen-independent prostate cancer (AIPC) patients treated at M.D. Anderson and several of its community oncology affiliates, 2 drug regimens were shown by randomized phase II analysis to be comparable. These regimens were ketoconazole/doxorubicin alternating with vinblastine/estramustine (KA/VE) or paclitaxel, estramustine, and oral etoposide (TEE). Both produced survival advantage when compared to prior series, including those in which mitoxantrone and prednisone were used. However, there was significant observed toxicity, particularly in the community-enrolled patients. Thus, although it is encouraging to see that chemotherapy can influence the natural history of this disease, more effective and tolerable regimens are sought.*

Source: Millikan R, et al. *J Clin Oncol*. 2003;21:878-883.

Androgen-independent prostate cancer (AIPC) is recognized as a highly aggressive disease associated with significant morbidity and a median survival of less than 1 year.[1] Currently, the only FDA-approved regimen for AIPC is mitoxantrone and prednisone, but reports suggest overall survival is no better with this approach.[1] However, a number of single-agent phase II trials[2] and a smaller number of combination chemotherapy reports[3] have suggested that the natural history of AIPC may be altered.

In the current report, Millikan and colleagues from M.D. Anderson with active collaboration from affiliated community oncology programs, report on a randomized phase II study of 2 different chemotherapy regimens for AIPC. The first was ketoconazole adriamycin alternating with vinblastine/estramustine (KA/VE) and the second was paclitaxel, estramustine, and oral etoposide (TEE). Patients were prospectively stratified on the basis of disease volume. The primary end points were response and overall survival time.

Of the 75 registered patients, 71 were eligible for analysis.

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Using criteria of an 80% prostate-specific antigen (PSA) reduction maintained for at least 8 weeks, 11 (30%) of 37 patients in the TEE arm responded, whereas 11 (32%) of 34 assigned to KA/VE responded. Median survival was 16.9 months (95% confidence interval [CI], 10.5-21.2 months) in the TEE arm and 23.4 months (95%CI, 12.9-30.6 months) for patients treated with KA/VE. Many patients (24%), particularly those treated at community sites rather than at the tertiary referral center, were unable to complete the initial 6 weeks of chemotherapy (either regimen). There were 5 (8%) treatment-related early deaths.

Millikan et al concluded that both regimens produced significant response rates but with moderate toxicity, particularly for those treated at community sites. They suggested that the improved overall survival (18.9 months for all 71 patients) when compared to prior series is an indication of the potential for combined chemotherapy to influence the course of AIPC but that newer, more tolerable regimens be developed before a large-scale, phase III study be undertaken.

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EDITORIAL GROUP HEAD: Glen Harris.
MARKETING PRODUCT MANAGER: Schandale Kornegay.
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Editorial E-Mail Address:
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COMMENT BY WILLIAM B. ERSHLER, MD

In the community setting, particularly among urological surgeons, there remains a sense that once prostate cancer becomes refractory to hormonal intervention, there is little useful therapy other than analgesics. Although the mitoxantrone/prednisone combination has been widely used, its approval by the FDA was based on an improved quality of life without demonstrated survival benefit. The current report hopefully will diminish this sense of therapeutic nihilism inasmuch as median survival for the treated AIPC patients (18.9 months) exceeded that from previous reports (eg, 7.9 months for mitoxantrone/prednisone).

In the design of this protocol, it is of particular interest to notethe effort made to recruit and retain community patients on study. Recruitment of patients in the community turned out to be more difficult than anticipated. Milliken et al speculated that this may reflect a sense the drug combinations were either too complex or toxic. Also, both arms included oral chemotherapy (estramustine, etoposide), which might have presented financial obstacles, particularly for those who rely on Medicare without supplemental prescription coverage.

Thus, the entire treatment group included those treated at M.D. Anderson and those treated in community practice affiliates. There was more toxicity, more withdrawals from study, and greater mortality observed in the community-treated patients. This observation is important to consider and requires explanation. Millikan et al speculate that it has more to do with patient selection (with younger patients with better performance status more likely to be treated at the cancer center) than other management issues. However, it is difficult to become too enthusiastic about selecting either of these comparable regimens for use in the community, in light of the burden of the schedule and the not insignificant treatment-related morbidities and mortality in this setting. Yet, it is apparent that combination chemotherapy will offer survival benefit to those with AIPC. However, we clearly need more community-based research protocols or more academic center protocols that include patients who better reflect what is seen in the community before community oncologists will be observing treatment advances for this disease. ■

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Prognostic Factors for Patients with Advanced-Stage Serous Borderline Tumors of the Ovary

ABSTRACT & COMMENTARY

Synopsis: *In this series, the only prognostic factor for patients with advanced-stage borderline tumor is the type of peritoneal implant. More patients died of the treatment's complications than of the disease itself. The patients' prognosis with noninvasive implants seems to be excellent, and conservative management could be discussed in younger patients.*

Source: Morice P, et al. *Ann Oncol.* 2003;14:592-598.

The ovarian malignancy, low malignant potential ovarian tumors (LMPOT) are defined by an epithelial tumor with a stratification of the epithelial lining, but with a lack of frank stromal invasion at pathological examination. It has a much less aggressive behavior than typical invasive epithelial ovarian cancer. The prognosis of patients with disease limited to the ovaries is excellent, but there are some patients with extra-ovarian spread. The histologic subtype is also important, as patients with mucinous borderline tumors and peritoneal extension (pseudomyxoma peritonei) are different. LMPOT account for approximately 15% of epithelial ovarian cancers with approximately 4000 patients diagnosed annually. The average age is 49 years, with the highest frequency of cases occurring in the 15-29 age group. These tumors may occur in a background of benign neoplasia and/or in association with areas of invasive disease.[1] Therefore, a thorough sampling of the primary tumor is critical to the establishment of an accurate diagnosis. The term "microinvasion" has been applied to cases that appear to bridge the definitions of LMPOT and invasive lesions. The prognosis is similar to noninvasive lesions.[2]

COMMENT BY STUART M. LICHTMAN, MD, FACP

This paper is a current review of a series including patients with advanced-stage serous borderline tumors of the ovary. This is the second largest series of patients with advanced-stage LMPOT. Their charge was to determine the prognosis of patients with serous LMPOT associated with peritoneal implants, as well as proposing an adequate treatment for these patients. The results were an analysis of 80 patients with a median age of 32 years. Most patients had elevated CA125 levels with a mean of 183 U/L. Twenty-nine patients had stage II disease, and 51 had stage III disease. Sixty-five patients had noninvasive implants, and 15 had invasive implants. Sixty-five patients had what was considered radical surgery, and 46 received some form of adjuvant treatment. This included radiation in 6 patients and chemotherapy to 32 patients. In 8 patients both treatments were given. Twenty-six of the chemotherapy patients received a platinum-containing regimen. Fifteen patients had recurrences with a median delay for recurrences of 23 months. Six patients had peritoneal recurrences with invasive disease. Four were observed in the patients with invasive implants and 2 in the patients with noninvasive implants. Their analysis showed that the rate of developing invasive disease is related to whether the patients had invasive peritoneal implants and the time of initial diagnosis (31% with invasive vs 2% with noninvasive; $P < .002$). Another entity has been described in patients with peritoneal implants associated with borderline tumor called micropapillary serous carcinoma (MPSC). It is more often, but not exclusively, associated with invasive implants.

In this study, the presence of stromal microinvasion was not an adverse prognostic factor. However, the rate of recurrence is increased (23% vs 3.5%; $P = .023$). In another review, the overall survival of patients with microinvasion is 100%.[3] Morice and colleagues concluded that in patients with a good prognosis (borderline ovarian tumor with noninvasive implants) conservative surgery and total resection of the peritoneal implants were warranted. The role of chemotherapy is questionable and in some series more patients died from complications of the adjuvant treatment than from progression of the disease. In patients with invasive implants Morice et al have recommended chemotherapy after surgery.

This paper discussed a histologic subtype of malignant ovarian tumors, which is often not diagnosed. Recognition of this clinical syndrome is important, as patients generally have an excellent prognosis usually with the need for chemotherapy. This will avoid overtreatment in this generally younger patient population. The clinicians must work in closed association with the pathologist to ensure an accurate diagnosis. Conservative management seems appropriate in the vast majority of cases. The increased relapse rate of invasive implants may make one consider adjuvant chemotherapy. However the true benefit of these treatments has not yet been proven. ■

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Radiotherapy Alone for Primary Cutaneous B-cell Lymphoma

ABSTRACT & COMMENTARY

Synopsis: *There are no well-defined guidelines for the treatment of primary cutaneous B-cell lymphoma (PCBCL). Since it is an uncommon diagnosis, it is unlikely that answers will come from randomized trials. This retrospective study from 2 German centers evaluated outcomes from a cohort of 35 patients and concluded that radiotherapy to all visible lesions is the treatment of choice.*

Source: Eich HT, et al. *Int J Radiat Oncol Biol Phys*. 2003;55:899-906.

Skin is the second most common extranodal location for B-cell lymphoma, after the gut. Primary cutaneous B-cell lymphoma accounts for approximately 5% of all cutaneous lymphomas in the United States. Low-grade subtypes are the most prevalent. According to the 1997 EORTC classification, these would be the follicle center cell (FCCL) and immunocytoma subgroups. Large B-cell lymphoma of the leg (LBCLL) is an intermediate subtype, and plasmacytoma and intravascular B-cell lesions are provisional subtypes.[1] PCBCL can present in a variety of ways, and it may take years before a definitive diagnosis is established. Lesions can appear as nodules, papules, or plaques that are usually reddish to livid in color. Eich and colleagues combined data from the Universities of Cologne and Muenster in order to retrospectively evaluate results of therapy.

From 1984 to 2001, 35 patients were treated with primary radiotherapy. All patients with a diagnosis of PCBCL were referred without selection. Median age was 61 years (range, 27-86 years). Sixty-percent of patients had FCCL (n = 21), 20% had immunocytoma (n = 7), 11% had LBCLL (n = 4), and 9% had a provisional variety (n = 3). Thirty-seven percent of patients presented with lesions on their head and neck (n = 13), 23% each on the trunk and lower extremities (n = 8 each), and 17% with PCBCL on their arms (n = 6). Most patients (n = 18, 51%) presented with a single tumor, but 35% (n = 10) had multiple tumors in 1 anatomic region, and 20% (n = 7) had lesions in noncontiguous sites. Lesions varied from 0.5-15 cm in greatest diameter.

The majority of patients received RT alone (n = 29, 83%). The remainder underwent surgery first. All except 2 patients were treated with 5-12 MeV electrons. Two patients were treated with photons, and 1 received mixed photon/electron therapy. Margins on the tumors were > 2 cm for lesions on the head/neck, and 5 cm for lesions on the trunks/extremities. Median dose was 45 Gy (range, 16-54 Gy). Median dose per fraction was 1.8 Gy (range, 1.8-3 Gy). Bolus material was used to bring the dose to the surface of the skin where needed. Electron treatments were prescribed to the 95% isodose line.

All 35 patients, except for 1 whose lesion involved an entire leg and who died after 16 Gy of pneumonia, achieved a complete response to therapy. Treatment was well tolerated in all patients. Median follow-up was 52 months. Median overall survival was 115 months for the entire group, and 5-year actuarial overall survival was 75%. Mean disease-free survival was reported as 77 months, and 5-year actuarial DFS was 50%. At the end of the study period, 27 patients were alive, 18 without disease, and 9 with disease. Three died of disease, and 8 died of other causes. There were 11 cutaneous relapses (31%) after a median of 11 months (range, 3-24 months), 3 of which were in or at the margin of the RT field. Of these, 2 were salvaged with either additional RT or with chemotherapy. Eight patients recurred in skin outside the primary field, and 5 were salvaged with RT, while 3 exhibited progressive disease on chemotherapy. There were no extracutaneous recurrences at first relapse.

Multivariate analysis evaluated age, gender, primary site, histologic subtype, and number of lesions for prognostic significance. Two or more noncontiguous anatomic sites of disease and LBCLL were noted to be independent unfavorable factors.

Eich et al concluded that a total dose of > 40 Gy with > 2-3 cm margins encompassing all visible lesions is the treatment of choice in all patients except PLBCLL, where chemotherapy is advisable. Multifocal skin disease is not an indication for chemotherapy except in the latter subtype.

COMMENT BY EDWARD J. KAPLAN, MD

Bekkenk and associates published their experience with a variety of approaches for 29 patients with

PCBCL from the Dutch Cutaneous Lymphoma Group, and the conclusions were exactly the same as Eichs et al.[2] Their median follow-up was 50 months. In this study, 55% of patients had FCCL and 28% had the immunocytoma subtype, roughly the same proportions as in the German study.

In contrast to the Eich and Bekkenk studies, Sarris et al from MDACC came to a different conclusion.[3] Their retrospective analysis of 46 patients with primary cutaneous lymphoma treated from 1971-1993 contained a preponderance of diffuse large-cell lymphomas (n = 19). Forty-two of the 46 patients had aggressive lymphomas according to the REAL classification. Ten patients were treated with RT alone, and 33 received doxorubicin as part of their therapy. Two patients were not treated at all. The MDACC patients achieved a 90% complete response rate with RT, 100% with chemoradiation, and 88% with chemotherapy alone. At a median follow-up of 140 months, actuarial 12-year disease-free survival was 61%. Seventy-one percent of the diffuse large-cell lymphoma patients had no evidence of disease (NED) at 12 years compared with none who received RT alone ($P = 0.0003$). FCCL patients enjoyed an excellent 12-year NED rate following chemoradiation. Eich et al concluded that RT alone was not curative for cutaneous diffuse large B-cell lymphoma, and that further work needs to be done in order to define the optimal therapy for FCCL.

At first glance, Eich and the MDACC investigators' conclusions appear to be at odds with those of the 2 European studies. However, the differences can largely be explained by the patient mix. While the European groups were mainly composed of patients with indolent disease, the American study was heavily weighted toward aggressive lesions. All 3 studies were small. All 3 studies are probably justified in their conclusions. The German and Dutch researchers agreed that patients with large B-cell lymphoma of the leg were not candidates for RT alone, and certainly the MDACC researchers would agree. Whether chemotherapy is necessary for patients with FCCL is not known, but based on the European experience, it may not be required. It will be interesting to watch as more data accrue for patients with cutaneous B-cell lymphomas, but for now there seems to be general agreement that patients with high-grade lesions need chemotherapy integrated into their treatment program, while patients with low-grade disease may do well with RT alone, even in the setting of multiple lesions. ■

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A Phase II Study of Docetaxel in Paclitaxel-Resistant Ovarian and Peritoneal Carcinoma

ABSTRACT & COMMENTARY

Synopsis: *Docetaxel is active in paclitaxel-resistant ovarian and peritoneal cancer, but, in view of significant hematologic toxicity, further study is warranted to ascertain its optimal dose and schedule.*

Source: Rose PG, et al. *Gynecol Oncol*. 2003;88: 130-135.

Within the gynecologic oncology group, Rose and colleagues conducted this phase II study of a relatively new drug, docetaxel, which is a taxane agent (related to paclitaxel [Taxol]) that is an inhibitor of microtubule depolymerization and has demonstrated activity in paclitaxel-resistant breast cancer and gynecologic cancer. Sixty patients were entered and treated with a total of 256 courses, with all 50 evaluable for toxicity and 58 evaluable for response. Responses were observed in 22.4% of patients, with 5.2% achieving complete response and 17.2% achieving partial response. The median duration of response was 2.5 months. The likelihood of observing a response did not appear to be related to the length of the prior paclitaxel-free interval or duration of prior paclitaxel infusions. The principal adverse effect of grade 4 neutropenia occurred in 75% of patients. There was 1 treatment-related death. Dose reductions were required in 36% of patients. Rose et al concluded that docetaxel is active in paclitaxel-resistant ovarian and peritoneal cancer but also indicated that, in view of significant hematologic toxicity, further study is warranted to ascertain its optimal dose and schedule.

■ COMMENT BY DAVID M. GERSHENSON, MD

Like paclitaxel (Taxol®), docetaxel is a taxane drug that has activity against epithelial ovarian cancer. Randomized phase III trials have demonstrated that the combination of docetaxel + carboplatin has efficacy equivalent to the combination of paclitaxel + carboplatin in patients with newly diagnosed advanced

epithelial ovarian cancer. Importantly, docetaxel has considerably less associated neurotoxicity than paclitaxel but more myelotoxicity. Docetaxel is being used increasingly in the first-line setting in combination with carboplatin, and it is also being used more commonly in the recurrent setting. In general, most oncologists have preliminarily considered docetaxel and paclitaxel to be interchangeable in terms of activity. Similarly, if a patient has demonstrated tumor resistance to one of the taxane agents, it has been thought that resistance to the other taxane is likely (cross-resistance). In fact, this study demonstrates that there is not complete cross-resistance, since 22.4% of all patients with paclitaxel-resistant ovarian and peritoneal cancer who received docetaxel responded. As expected, neutropenia was the most bothersome side effect, but the starting dose of docetaxel in this study was 100 mg/m^2. Lower doses can ameliorate this toxicity. As Rose et al correctly note, the findings of this study clearly expand our armamentarium against ovarian cancer, but future studies will be required to establish the optimal dose and schedule for this interesting agent. ■

Dr. Gershenson is Professor and Chairman, Department of Gynecology, M.D. Anderson Cancer Center, Houston, Tex.

Women's Perceptions About Treatment Decision-Making for Ovarian Cancer

ABSTRACT & COMMENTARY

Synopsis: *Women with advanced epithelial ovarian cancer did not describe the treatment decision-making process as shared; rather, they described an interaction that was directed by their physician.*

Source: Elit L, et al. *Gynecol Oncol*. 2003;88:89-95.

Elit and colleagues conducted in-depth semi-structured interviews with 21 patients who underwent initial surgery for stage III or IV ovarian cancer and who had received less than 2 cycles of chemotherapy. Their analysis highlighted 5 themes:

1. **Knowledge of treatment benefits and risks.**
   Women understood that the treatment had both survival and quality-of-life benefits. Women could clearly articulate the risks of chemotherapy.
2. **Readiness to make a decision.**
   When making treatment decisions, women described being overwhelmed by the effects of concurrent drugs like analgesics, the severity of the illness, unexpected diagnosis of cancer and grief, and feeling pressured into a decision.
3. **Perception of a treatment choice.**
   Most women felt that they made their treatment decision; however, most women did not perceive that they had a treatment choice. Thus, treatment decision-making is really a process of coming to terms with the disease and the recommended treatment.
4. **Physician-patient relationship.**
   All women suggest that their doctor knew the right treatment for them, and they felt confident in their cancer physician.
5. **Social supports.**
   Women described supports through decision-making processes that included individuals who advocated for them, faith, and past experience with the cancer system. Hindrances to decision-making included people who were negative, the cancer label, and employers.

Elit et al concluded that women with advanced epithelial ovarian cancer did not describe the treatment decision-making process as shared; rather, they described an interaction that was directed largely by the physician. These women attribute this form of decision-making to their advanced age, severity of illness, immediate ramification of treatment choices, and lack of advocacy for a different model of interaction. They further concluded that the onus is on the physician to ensure that there is an environment for shared decision-making in the event that the patient is interested in such an interaction.

■ COMMENT BY DAVID M. GERSHENSON, MD

This study underscores the importance of the doctor-patient relationship surrounding the initial diagnosis of advanced epithelial ovarian cancer. Over the past 2 decades or so, this interaction has transitioned from a paternalistic attitude on the part of the physician toward the patient to an environment in which there is a shared decision-making process. Obviously, from the reading of this article, there is still much room for improvement. A new diagnosis of advanced ovarian cancer is generally very devastating, and there is an expected feeling of "loss of control" for the patient and her family. Because the standard management for a woman with suspected advanced ovarian cancer is primary cytoreductive surgery followed by combination chemotherapy, patients may feel that their options are very limited. One strategy for broadening treatment options for patients is to be able to offer

innovative clinical trials, and much more work is needed to extend clinical trials into more community based practice settings. Elit et al use the comparison of this scenario to that of women with early stage breast cancer, who are more easily able to assume a more autonomous role in decision-making regarding their treatment. There are several reasons for this disparity, including differences in average age, general condition, and the influence of prognosis on psychological well-being. Much more study is needed in this area, but we are continuously moving closer to the ideal in which patient preferences emerge as key components during this most sensitive time. ■

Dr. Gershenson is Professor and Chairman, Department of Gynecology, M.D. Anderson Cancer Center, Houston, Tex.

Reducing Mortality in Sickle Cell Disease with Hydroxyurea

ABSTRACT & COMMENTARY

Synopsis: *Participants in the initial Multicenter Study of Hydroxyurea in Sickle Cell Anemia (MSH) interventional trial were followed, upon completion of that trial for up to 9 years, to determine the long-term effects of treatment. In this publication of the observational phase of the MSH trial, there is noted a 40% reduction in mortality for those who had received a year or more of the drug.*

Source: Steinberg MH, et al. *JAMA*. 2003;289; 1645-1651.

Hydroxyurea increases the level of fetal hemoglobin (HbF)[1] and decreases morbidity from vaso-oclusive complications in patients with sickle cell anemia (SCA).[2,3] In fact, epidemiological studies have shown that HbF concentration is the strongest determinant of clinical severity of sickle cell disease.[4-6] Thus, a large, multicenter, placebo-controlled trial was conducted between the years 1992-1995 (The Multicenter Study of Hydroxyurea in Sickle Cell Anemia [MSH]), which confirmed a reduction in morbidity (particularly veno-occlusive events) in patients with SCA. In the hydroxyurea treatment group (n = 152), there was a 44% reduction in the annual number of painful episodes and a 58% decrease in the number of cases for which hospitalization was required.[7] That trial was the basis for the Food and Drug Administration's approval of hydroxyurea for patients with recurrent moderate-to-severe painful crises associated with SCA.

The objective of the current research was to determine whether hydroxyurea treatment attenuates mortality in SCA patients. For this, survival of the participants in the MSH trial was recorded. These participants, upon completion of the formal trial, either chose to stay on hydroxyurea, be switched on to hydroxyurea (if they had received placebo during the interventional trial), or be treated with supportive measures alone, without hydroxyurea.

Of the original 299 patients who had participated in the MSH trial (hydroxyurea treated, n = 152; placebo, n = 147), follow-up data were available for up to 9 years on 233 (77.9%). Ninety-six (32%) of the patients never received hydroxyurea; 48 (16%) received hydroxyurea for less than 1 year, and 156 (52%) received hydroxyurea for 1 or more years.

Twenty-five percent of patients (n = 75) who were originally enrolled in the MSH trial have died. The most common cause of death (28%) was pulmonary disease. The cumulative mortality at 9 years was 28% when HbF levels were lower than 0.5 g/dL after the trial was completed compared with 15% when HbF levels were 0.5 g/dL or higher (P = 0.03). Individuals who had acute chest syndrome during the trial had 32% mortality compared with 18% of individuals without acute chest syndrome (P = 0.02). Taking hydroxyurea was associated with a 40% reduction in mortality (P = 0.04) in this observational follow-up.

COMMENT BY WILLIAM B. ERSHLER, MD

Since the publication of the MSH trial results, hematologists have been aware of the therapeutic benefit of hydroxyurea for those sickle cell patients with moderate or severe disease, particularly in reducing the frequency of painful crises and hospitalizations. The current follow-up provides the first data on survival, and the results are encouraging. Adult SCA patients (who had moderate-to-severe disease at the time of entry into trial, as defined by 3 or more painful crises/year) were shown to have reduced mortality after 9 years of follow-up. Furthermore, patients appeared to tolerate hydroxyurea well and not have increased long-term adverse consequences. There were 3 cancers observed in those receiving hydroxyurea, and only 1 proved fatal.

The questions remain, however, as to just who should receive hydroxyurea (those with mild, moderate, or only those with severe SCA?), at what age should treatment be started, and will this somewhat expensive medicine

be available for all those who could benefit from it? Additional clinical trials and health services research will be paramount to addressing these questions. ■

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CME Questions

17. Which of the following statements about hydroxyurea treatment for sickle cell anemia is *not* true?

a. Treated patients have been shown to have increases in HbF.
b. Treated patients have been shown to have reduced incidence of painful crises.
c. Treatment has been shown to reduce mortality, but only for those with mild disease.
d. Treatment has been shown to reduce mortality, but only for those with moderate-to-severe disease.

18. With regard to the treatment of androgen-independent prostate cancer, which of the following statements is true?

a. The ketokonazole/doxorubicin alternating with vinblastine/estramustine (KA/VE) regimen was demonstrably superior to the paclitaxel, estramustine, etoposide regimen (TEE) with regard to response rate and survival.
b. The KA/VE and TEE regimens were comparable and resulted in improved survival when compared to prior series.
c. The KA/VE and TEE regimens were comparable but offered no significant su;rvival advantage when compared to mitoxantrone-prednisone patients (historical controls).
d. The TEE regimen was demonstrably superior to the KA/VE regimen with regard to response rate and survival.

19. Which of the following statements is best supported by data from the 3 PCBCL studies discussed above?

a. Complications from therapy were commonly encountered.
b. First recurrences tended to be extracutaneous.
c. Indolent lymphomas do best with chemoradiation.
d. Diffuse large B-cell lymphomas tend to do the worst, especially if treated with RT alone.

Answers: 17 (c); 18 (b); 19 (d)

In Future Issues: **Using Gene Expression Ratios to Predict Clinical Outcomes**