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INSIDE

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Imatinib Improves Outcomes in Elderly Patients with Ph+ ALL

ABSTRACT & COMMENTARY

By William B. Ershler, MD

Synopsis: *Acute lymphocytic leukemia (ALL) in the elderly is not common, but as in younger adults, a subset will be Philadelphia chromosome postitive (Ph+). In young patients with Ph+ ALL, the addition of imatinib has been shown to be effective in enhancing complete response rates and relapse-free survival. The treatment of elderly patients with ALL has not been satisfactory and in this study, for those with Ph+ disease, imatinib was added to the consolidation (or salvage) phase in the overall initial treatment plan. The experience in 30 Ph+ ALL patients older than age 55 was compared by this group of French and Belgian clinical investigators to a series of 18 similar patients previously treated by an analogous protocol but without the imatinib. At the end of one year, relapse-free survival was 58% in the current cohort, which compared favorably with 11% of the historic controls. Thus, imatinib, used during consolidation may benefit older patients with Ph+ ALL.*

Source: Delannoy A, et al. Imatinib and methylprednisolone alternated with chemotherapy improve the outcome of elderly patients with Philadelphia-positive acute lymphoblastic leukemia: results of the GRAALL AFR09 study. *Leukemia*. 2006;20:1526-1532.

With advancing age there is increasing prevalence of Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ALL). In young patients with Ph+ALL, the addition of imatinib has been shown to be both safe and effective as an adjunct to chemotherapy.[1] In the current clinical trial conducted by a consortium of French and Belgium investigators, older patients (55 years and older) with de novo ALL were treated with a combination of initial chemotherapy followed by imatinib as consolidation, maintenance or salvage.

Over an approximate two-year period, 30 eligible (older than 55 years old, documented previously untreated Ph+ ALL) were enrolled in this trial conducted by the Group for Research on

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Adult Lymphocytic Leukemia (GRAALL). A complex treatment protocol was used that extended treatment over approximately two years. An induction phase consisted of chemotherapy (daunorubicin, vincristine, methylprednisilone) and irrespective of initial response, patients were then given consolidation/salvage therapy including imatinib 600 mg daily and steroids. Only patients in complete remission (CR) after the consolidation/salvage phase were offered to proceed with the maintenance therapy which included several 2-month blocks of chemotherapy and two additional 2-month blocks of imatinib. Treatment response for the included 30 patients was compared to that of 21 historical controls who were similarly aged and treated similarly but without added imatinib.

Of the 29 evaluable patients, 21 (72%) were in CR after induction chemotherapy vs 6/21 (29%) in controls. Five additional CRs were obtained after salvage with imatinib and four after salvage additional chemotherapy in the control group. Overall survival (OS) was 66% at 1 year vs 43% in the control group ($P = 0.005$). The 1-year relapse-free survival was 58% vs 11% ($P = 0.003$). Thus, these investigators concluded the use of imatinib was an effective adjunct to standard chemotherapy for Ph+ ALL occurring in elderly patients.

COMMENTARY

Curiously, the relative portion of ALL that is Ph+ increases with age through early adult years, but seems to decline again in late life. Imatinib, an orally administered inhibitor of the BCR/ABL encoded tyrosine kinase, has been demonstrated to be active in patients with Ph+ ALL in patients with relapsed or refractory disease. In one series, 29% of such patients obtained complete hematological remission.[1] Accordingly, imatinib has been effectively incorporated into the front line therapy in young adults with previously untreated Ph+ ALL.[2,3]

Unlike that for younger patients, the presence of the Ph chromosome is of little prognostic consequence in elderly ALL patients, most likely due to the overall poor prognosis of ALL in this age group.[4] Thus, a therapeutic advance, particularly one that is fairly well tolerated in this age group, is a welcome advance.

The current trial demonstrated the safety of incorporation of imatinib into the treatment regimen. Patients, in general, did better than historic controls, but it should be noted that there was a significantly higher CR rate during the induction phase for those on this trial than the controls, and it should be emphasized that imatinib was only used during the consolidation/salvage phase. Nonetheless, for those who did not achieve remission during induction, consolidation that included imatinib and steroids proved successful in 5 of 6 patients, whereas salvage chemotherapy was successful in only 4 of 12. Furthermore, overall survival was clearly improved by imatinib (median survival, 23.2 months compared to 11.2 months for the control group) and this would seem a reliable indicator of the efficacy of this consolidation/maintenance approach. Of course, ALL is not common in older people and Ph+ ALL comprises less than 25% of the total ALL population. Thus, a large scale cooperative group trial would seem the only likely mechanism to definitively establish the role for imatinib in the treatment of ALL in the elderly. ■

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Outpatient Azacitidine for Selected AML Patients

ABSTRACT & COMMENTARY

By William B. Ershler, MD

Synopsis: *A review of twenty AML patients who were treated with azacitidine demonstrated a response rate of 60% and for those that responded, a median survival of 15+ months. Patients included were those who were initially considered to have myelodysplastic syndrome (refractory anemia with excess blasts) or acute leukemia but unsuitable for more intensive chemotherapy. Azacitidine was administered by daily subcutaneous injection (out patient) for seven days, repeated monthly. Although generally well tolerated, four patients required hospitalization during the first cycle and infection occurred on 8 occasions. Single-agent, outpatient azacitidine may prove to be a useful treatment choice for selected patients with AML.*

Source: Sudan N, et al. Treatment of acute myelogenous leukemia with outpatient azacitidine. *Cancer*. 2006;107: 1839-1843.

Azacitidine has been used clinically to treat both myelodysplastic syndrome (MDS) and acute myelogenous leukemia (AML). When used to treat MDS, the dose and schedule is different, typically with lower doses administered subcutaneously for seven days, repeated monthly. For AML, azacitidine is usually given in larger doses, intravenously. Although clearly active, its use has been limited by toxicity. Investigators at the Western Pennsylvania Cancer Institute have reviewed their experience with azacitidine given to 20 patients who were either treated for MDS, but under current classification schemes would be considered to have AML (n = 12) or to patients with AML but for whom standard intensive chemotherapy was considered too risky (n = 8).

The overall response rate was 60%; complete responses occurred in 4 (20%), partial response in 5 (25%) and hematologic improvement in 3 (15%). The median survival of responders was 15+ months compared with 2.5 months in nonresponders. During therapy, responders had an ECOG performance status of 0 to 1. The most common toxic event was infection (n = 8) but four patients (20%) required hospitalization during the first cycle of treatment.

COMMENTARY

Less-than-intense therapy for AML has usually proven to be of little benefit in terms of remission induction, survival or quality of life. Low-dose cytosine arabinoside, for example, was commonly used for AML in high-risk patients, such as the elderly, but studies revealed little added benefit and definite toxicity.[1,2] Azacitidine, a derivative of the nucleoside cytosine, is a cell cycle specific agent which, when incorporated into DNA produces a marked decrease in activity of DNA methyltransferase.[3] In vitro exposure of leukemia cells resulted in differentiation, presumably due to the hypomethylation of DNA.[4] When administered in high doses, it has demonstrable activity in patients with AML with an overall response rate of 27% and remission duration of just over 100 days.[5] When given subcutaneously at lower doses, the drug has proven effective in MDS, with response rates approximating 60%.

Elderly patients with AML are a challenge.[6] For those with excellent performance status, standard intensive chemotherapy and even allogeneic transplant have been effectively used. However, the majority of elderly patients, particularly those older than 70, have existing comorbidities and/or functional impairments that preclude the safe use of such an intensive approach. Because the median age for AML is older than 60 years, it is an imperative that more effective and less toxic treatments be developed.

Azacitidine may well be a cornerstone of future treatment strategies for elderly AML patients. The current report suggests that when administered on a typical MDS-like schedule, it is relatively safe and somewhat effective. The fact that the majority responded and maintained an ECOG performance status of 0 to 1 is notable. However, complete remissions were few, survival for non responders was dismal (2.5 months) and the analysis was of insufficient duration to be confident about overall response duration. Certainly, we have a way to go in providing effective management for AML in the elderly. Also of consideration is the population studied. The majority of patients had a smoldering picture with the average time interval between diagnosis and chemotherapy of 11 months (range, 1 to 48 months). Thus, although in using the current WHO classification scheme, these patients had AML, at least some had a smoldering picture not entirely typical for AML. Nonetheless, azacitidine administered subcutaneously was shown to have activity in these patients and the relatively low toxicity profile and subcutaneous route of administration make it an appealing choice for some patients with this disease. Hopefully, additional agents will be developed that will enhance treatment success in this setting.

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AMG 531 Promotes Thrombopoiesis in ITP

ABSTRACT & COMMENTARY

By Andrew S. Artz, MD

Section of Hematology/Oncology, University of Chicago

Dr. Artz reports no financial relationship to this field of study.

Synopsis: *ITP is usually a chronic condition in adults resulting from both platelet destruction and impaired production. This study summarizes the early phase experience in two trials for chronic refractory ITP of AMG 531, a novel thrombopoiesis stimulating protein. Among the 41 patients in total treated at a variety of doses given every 1-2 weeks, 68% showed a good response. No serious side effects occurred. AMG 531 appears promising as a thrombopoiesis stimulating agent in chronic ITP.*

Source: Bussel JB, et al. AMG 531, a Thrombopoiesis-Stimulating Protein, for Chronic ITP. *N Engl J Med.* 2006;355:1672-1681.

IMMUNE THROMBOCYTOPENIC PURPURA (A/K/A/ Idiopathic Thrombocytopenic Purpura or ITP) is an acquired platelet disorder diagnosed by exclusion.[1] The biology of ITP is heterogeneous. Interestingly, not only is there accelerated platelet destruction but also impaired megakaryopoiesis. Clinically, ITP is a characterized by mucocutaneous bleeding and a chronic course. A variety of treatments may be used as initial therapy, including glucocorticoids, IGIV and Anti-D (WinRho). Treatment for relapsed disease may incorporate any treatment employed as initial therapy as well as splenectomy, rituximab, other immunosuppressive agents, and even autologous stem cell transplantation.

The low incidence of serious bleeding from ITP 2 and considerable complications arising from therapy requires clinicians to exercise extreme caution in treatment. For example, chronic steroids can have devastating long-term toxicities. Authorities generally recommend avoiding treatment for chronic asymptomatic ITP with a platelet count above 30,000/uL. More effective and/or less toxic treatment alternatives are sorely needed, particularly for severe chronic ITP. Bussel and colleagues report promising results from an early phase clinical trial of a novel thrombopoiesis stimulating agent in patients with chronic ITP.

The report summarizes data of two studies across nine US institutions employing AMG 531, a novel thrombopoiesis stimulating protein. Eligibility criteria included age 18-65 years, ITP for at least 3 months, at least one line of prior therapy, and a platelet count of < 30,000/uL or < 50,000/uL for those on corticosteroids. The first study was an open-label, dose-escalation trial where AMG 531 was administered once subcutaneously and patients followed for 14 days and then a second dose could be considered. The second study was a double-blind, placebo-controlled study (4:1 assignment favoring AMG 531) where the study drug was administered once weekly for six weeks.

In the first phase, 24 patients were enrolled in six dose cohorts with a median platelet count of 11,000/uL. Twenty-one patients were enrolled in phase 2, of which 17 were assigned to AMG 531. The majority had previously undergone a splenectomy (79% in phase 1 and 67% in phase 2). No serious adverse events appeared related to AMG 531 although in some patients the platelet count fell lower than baseline transiently after discontinuing therapy. No antibodies to AMG 531 or thrombopoietin were detected. The overall response rate was 68% of achieving a platelet count > 50,000/uL and usually occurred within a week of therapy. In those receiving the 1 ug and 3 ug doses in the phase 2 portion, the mean platelet counts were 135,000/uL and 241,000/uL compared to 81,000/uL for placebo.

COMMENTARY

Bussel and colleagues report intriguing data employing AMG 531, a novel thrombopoiesis stimulating mol-

ecule exhibiting a protein structure unique from thrombopoietin. In the combined results of the phase 1 and 2 portions, ultimately 41 patients with chronic refractory ITP were treated at a variety of doses. A platelet count above 50,000/uL occurred in 68% of patients including those on the dose escalation portion.

While this trial evaluated only a small number of patients, the results are noteworthy in several respects. The study documents clinical activity employing a thrombopoiesis stimulating protein in ITP. Therapy aimed at increasing production is a dramatic departure from present therapies focused primarily at reducing platelet destruction. The study builds upon prior results using PEG-MGDF, a recombinant form of thrombopoietin. In early studies, PEG-MGDF improved platelet counts but also caused antibodies against thrombopoietin, leading to severe thromobocytopenia and cessation of drug development. In this study, no antibodies to AMG 531 or thrombopoietin were detected. Longer follow-up with repeated drug administration of AMG-531 will be needed to ensure antibodies do not develop. The fall in platelet count after drug discontinuation, presumably from reduced thrombopoietin levels as the megakaryocyte mass was expanded, necessitates further study as well.

ITP remains a challenging condition. While some patients may not require therapy, a subset either don't respond to therapy or more often have serious consequences from long-term treatment that may pose a more serious risk than bleeding from ITP. An agent working via a different mechanism, such as enhanced production, if safe, could play an important role in chronic refractory ITP as either a treatment alternative, or as a treatment adjunct.

The data derived from early phase studies hold promise but clearly requires much more clinical testing to determine an appropriate dose, ensure safety, and validate efficacy. We must also be cognizant that as a novel recombinant protein with a short duration of action, it would likely have considerable costs and require frequent drug administration. Whether AMG 531 will have a role in other conditions, such as chemotherapy induced thrombocytopenia, remains unknown. In conclusion, AMG 531 has activity in chronic refractory ITP warranting further testing. ■

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Adjuvant Chemotherapy (Yes or No) After Colorectal Liver Metastases Resection

ABSTRACT & COMMENTARY

By William B. Ershler, MD

Synopsis: *The question of the role for systemic therapy in addition to surgical resection of liver metastases was addressed by Portier and colleagues from France by conducting a multicenter trial in which 173 patients with liver-only colorectal metastases had resection of the metastatic lesion(s) with or without additional systemic chemotherapy (fluorouracil and leucovorin). The 5-year disease-free survival rate of 33.5% for those receiving adjuvant therapy was significantly better than that for the surgery-only arm (26.7%).*

Source: Portier G, et al. Multicenter randomized trial of adjuvant fluorouracil and folinic acid compared with surgery alone after resection of colorectal liver metastases: FFCD ACHBTH AURC 9002 trial. *J Clin Oncol*. 2006;24: 4976-4982.

There has remained some controversy on the advisability of systemic chemotherapy after resection of hepatic metastases from colorectal cancer. This, despite the demonstrated benefit of such in patients at high risk for recurrence after primary surgery or in those with stage IV disease. Yet, there had previously been no randomized clinical trial demonstrating benefit in terms of overall survival. In the current multicenter trial, 173 patients with completely resected hepatic metastases from colorectal cancer were randomized to surgery alone (observation, n = 87) or to surgery followed by 6 months of systemic adjuvant chemotherapy with fluorouracil and folinic acid (n = 86). Using an intention-to-treat analysis (171 patients evaluable), after a median follow-up of 87 months, the 5 year disease free survival rate was 33.5% for the patients in the chemotherapy group and 26.7% for patients in the control group (Cox multivariate analysis: odds ratio for recurrence or death = 0.66; 95% CI, 0.46-0.96; $P = 0.28$). With regard to secondary outcome measures, a trend towards increased overall survival was observed but did not reach statistical significance (5-year overall survival: chemotherapy group, 51.1% vs control group, 41.1%; odds ratio for death, 0.73; 95% CI, 0.48-1.10; $P = 0.13$).

Thus, adjuvant systemic chemotherapy provided a significant disease-free survival benefit for patients with

resected liver metastases from colorectal cancer.

COMMENTARY

Although chemotherapy may prolong survival in patients with hepatic recurrence of colorectal cancer, surgical excision offers the best and probably only chance for cure. Recent developments in radiofrequency ablation (RFA) and similar approaches are also likely to offer comparable results in selected patients. Yet, even with effective surgery or RFA, a substantial portion of the patients recur, either in the liver or at other sites. Accordingly, it would seem that such individuals would be excellent candidates for adjuvant therapy. However, only two randomized phase III trials in which the comparative group was surgery alone have been published,[1,2] and the results of these were not definitive. In one of these, hepatic arterial infusion (HAI) of floxuridine (FUDR) or fluorouracil compared with either surgery alone or systemic therapy showed a recurrence free benefit of chemotherapy over surgery alone. However, this trial was not designed to assess an overall survival benefit. In the other trial, HAI of FU plus leucovorin was compared to surgery alone, and no benefit beyond surgery was observed.

The current report is the first adequately powered trial comparing systemic chemotherapy after surgery to surgery alone. The trial was projected to enroll 200 subjects, but was closed after ten years with only 173, due to slow accrual. Using disease-free survival as the primary end point, patients receiving postoperative chemotherapy fared significantly better than those receiving surgery alone. There was also a trend toward benefit in overall survival, though this had not reached a level of statistical difference.

In his editorial comments regarding this trial,[3] Alberts highlights the problems that can occur in a trial that is slow to accrue, including the point that the chemotherapy used would be considered inferior to current standards that might include such agents as oxaliplatin, irinotecan, bevacizumab, or cetuximab. He points to the fact that the trial showed benefit with FU and leucovorin as a proof in concept that adjuvant therapy is useful in this setting, but that the trial needs to be validated using more modern systemic approaches. Fortunately, the EORTC trial 40983, in which patients with liver only colorectal metastases were randomly assigned to surgery alone or 3 months of oxaliplatin, leucovorin, and FU (FOLFOX4) before surgery and 3 months of FOLFOX 4 after surgery has recently completed its accrual of 300 patients, and overall survival is the primary end point.

Thus, it is likely that most experts today would agree that systemic adjuvant therapy is justified in the setting of hepatic resection of colorectal metastases. The question regarding the drugs to be administered and their scheduling remains unanswered, as does the impact of such an approach on overall survival.

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Therapeutic Role of Lymph Node Resection in Endometrioid Corpus Cancer

ABSTRACT & COMMENTARY

By Robert L. Coleman, MD

Associate Professor, University of Texas; M.D. Anderson Cancer Center, Houston

Dr. Coleman is on the speaker's bureau for GlaxoSmithKline, Bristol-Myers Squibb, and Ortho Biotech.

Synopsis: *The findings of the current study suggest that the extent of lymph node resection improves the survival of women with intermediate/high-risk endometrioid uterine cancer.*

Source: Chan JK, et al. Therapeutic role of lymph node resection in endometrioid corpus cancer: a study of 12,333 patients. *Cancer*. 2006;107:1823-1830.

The therapeutic role of lymphadenectomy in patients with endometrial cancer is controversial and challenging to study given the relative infrequency of metastatic disease and the generally good prognosis of newly diagnosed patients. Nevertheless, prior work in limited sized cohorts has suggested that the number of nodes resected may be prognostic and informative in planning subsequent adjuvant treatment. To address

these questions, Chan and colleagues evaluated over 12,000 women registered in the SEER database in whom nodal sampling accompanied their primary surgical procedure from 1988-2001. Patients with Stage I to IV disease and endometrioid histology (all grades) were included in the study cohort. Importantly, women with uterine serous histology and uterine sarcoma were excluded. In light of the large sample size, 5 categories of node counts could be evaluated. Risk groups were considered as well, defined as: Low Risk (Stage IA, all grades, Stage IB, Grade 1-2), Intermediate Risk/High risk (Stage IB, Grade 3, Stage IC-IV, all Grades) and High Risk (Stage IIIC-IV). The authors documented that the percentage of patients undergoing nodal sampling significantly increased over the years of the study (23% to 41%; $P < 0.001$). The number of nodes resected was significantly associated with improved survival for intermediate/high-risk and high-risk patients. No benefit in disease-specific survival was seen for the low-risk cohort. Age at diagnosis, race, year of diagnosis, grade, identified metastatic nodal disease, and adjuvant therapy were significant covariates in the study; however, in the multivariate analysis, node count remained a significant prognostic factor to disease specific survival in the intermediate/high-risk cohort after adjustment for these effects. The authors concluded that node count acts as a surrogate for extent of node resection and improves the survival of women with intermediate/high-risk endometrioid uterine cancer.

COMMENTARY

One of the most important prognostic factors for uterine cancer limited to the corpus is identification of extrauterine disease, particularly retroperitoneal adenopathy. Fortunately, the identification of metastatic disease occurs in just 1 in 5 women with endometrioid primary cancers. However, the price for undetected metastatic disease is high. This has led to two approaches or management philosophies regarding intervention: broader application of more extensive nodal sampling or more frequent utilization of adjuvant therapy in patients where staging information is missing. Both approaches have merit but risk overtreatment. The former strategy ensures accurate diagnostic information in all cases but 80% of women will receive limited benefit from the procedure; the latter, ensures high-risk areas are treated without the attendant morbidity of extensive surgery but does so blindly as the target volume is "guesstimated" (vaginal cuff and/or pelvis field and/or paraortic field). The current article provides some guidance to this dichotomous treatment approach for women with endometrioid tumors.

One relevant observation the authors identify is that there appears to be a cohort of patients (totaling 5,556/12,333 or 45% of the population) in whom nodal sampling or dissection offers no therapeutic value—patients with stage IA, all grades and stage IB, grades 1 and 2. Survival in this low-risk cohort ranges from 94% to 97%, irrespective of the extent of nodal resection. However, for all other risk cohorts, node count has a profound effect on survival. Most impressive is the effect of node count on patients with identified metastatic disease. Of 1221 patients with stage IIIC/IV disease, 5-year disease-specific survival ranged from 51% in women with 1 resected node to 72% in women with more than 20 resected nodes. To minimize sampling bias, they additionally evaluated the ratio of positive nodes to the total number of nodes resected. In this analysis women in whom the metastatic node ratio was greater than 20% had a survival of 51% compared to those in whom the number of metastatic nodes were 5% or less of the total node resection. While this kind of analysis can be confounded by misclassification of patients with high positive node counts, their specific occurrence is historically uncommon and may still be positively offset by more thorough lymphadenectomy.

The second point raised in this analysis is that patients without formal staging may be misclassified as having optimistic outcomes in apparent early stage disease and poor outcome in advanced stage disease. Women undergoing formal evaluation by lymphadenectomy resulting in an early stage (Stage I) designation similarly have favorable outcomes; however, the survival for those identified advanced disease (Stage II-IV) is substantially better. This result is likely the combination of stage migration and the therapeutic value of resection—even unaffected nodes. It also speaks to better defining the treatment volume of "at-risk" tissues, which has the potential to reduce treatment-related toxicity.

This current report suffers the fate of similar SEER-based analyses with inconsistent or absent central pathology review, missing data of adjuvant hormonal and chemotherapy, undefined skills of the surgeon, unknown progression-free survival and incomplete detail of subsequent therapy for recurrence. In addition, while node counts may serve as a surrogate of completeness of resection, it is highly operator-dependent. Large node counts can be achieved if they are specifically sought in gross processing, particularly if defattying agents are utilized. Reproducible criteria which ensure the completeness of resection are unavailable and probably better represented by specified sampling in specific nodal regions such as: external iliac, obturator, junctional, common iliac, low paraortic (below the inferior mesenteric artery) and

paraortic (ovarian). However, the data are provocative and are positive reinforcement for the trend identified in this study of a greater proportion of patients being referred for expert surgical care by trained gynecologic oncologists. ■

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CME Questions

23. Regarding adjuvant chemotherapy after resection of hepatic colorectal metastases, which of the following endpoints was statistically significant in the recent French cooperative study:
a. Disease free survival at 5 years.
b. Time to recurrence.
c. Overall survival.
d. All of the above.
e. None of the above.

24. In a small series of patients from Pittsburgh treated with single agent azacitidine for acute myelogenous leukemia, which of the following statemtments is true:
a. Approximately 60% achieved a complete remission (CR).
b. For those who achieved complete remission, physical function (as measured by ECOG performance Status) remained stable (ECOG 0 to 1).
c. Median survival for those who achieved CR was 9 months.
d. All of the above.
e. None of the above.

25. For elderly patients with Ph+ ALL, the addition of imatinib to the consolidation/salvage phase of initial therapy was shown, when compared to historic controls, to:
a. improve CR rate but have minimal effect on disease-free survival.
b. improve CR rate and enhance disease-free survival.
c. reduce CR rate but enhance disease-free survival.
d. reduce CR rate and reduce disease-free survival.

26. In this manuscript using AMG 531, a thrombopoiesis stimulating molecule, for chronic ITP, what did the authors find?
a. AMG 531 lead to more bleeding.
b. Antibodies did NOT develop to AMG 531 or thrombopoietin during the study.
c. AMG 531 was definitely more effective then rituximab.

Answers: 23 (a); 24 (b); 25 (b); 26 (b)

CME Objectives

The objectives of *Clinical Oncology Alert* are:

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- to present prevalence/surveillance data and long-term follow-up results of chemotherapy/radiation regimens; and
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