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HOPA News

Triple Threat? Expanded Frontline Options for Patients Newly Diagnosed with Chronic Myeloid Leukemia

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The results from the International Randomized Study of Interferon (IRIS) and STI571 trial in 2002 have contributed to imatinib becoming the standard of therapy for patients who are newly diagnosed with chronic myeloid leukemia (CML; National Comprehensive Cancer Network, 2010). Imatinib represents a major advancement in the management of patients with CML because it was the first tyrosine kinase inhibitor found to inhibit activity of the BCR-ABL kinase—an aberrant protein that is the product of the Philadelphia chromosome translocation (t(9;22)). Despite major improvements in outcomes for patients with CML using imatinib, as many as 15%–25% of them fail to achieve a complete cytogenetic response within the first 12 months of therapy.[1] Secondary treatment options, including dasatinib and nilotinib, represent next generation BCR-ABL tyrosine kinase inhibitors that were initially developed to overcome imatinib-resistant variants of BCR-ABL. Though dasatinib and nilotinib previously were demonstrated to be efficacious in this patient population, current research has been directed toward patients newly diagnosed with CML. In comparison to imatinib, dasatinib is 325 times more potent and nilotinib is 30 times more potent in inhibiting wild-type BCR-ABL in vitro.[2,3] The clinical impact of this increased potency has been discussed in two recent phase 3 trials that examined dasatinib and nilotinib versus imatinib in patients newly diagnosed with chronic phase CML.

The Dasatinib Versus Imatinib Study in Treatment-Naïve CML Patients (DASISION trial) represents the first phase 3 investigation that directly compares imatinib to dasatinib in 519 adults with newly diagnosed chronic phase CML.[3] Patients were randomized to receive dasatinib 100 mg once daily (n = 259) or imatinib 400 mg once daily (n = 260). No significant differences were found among each arm regarding demographics or distribution of disease burden per Hasford risk. The trial allowed for interruptions or dose modifications per standard practice for lack of response or toxicity. No information was provided regarding the frequency of dosage adjustments; however, the median dosage for the dasatinib arm was 99 mg/day (range = 21–136) versus 400 mg/day for the imatinib arm (range = 125–657). At the 12-month evaluation point, a complete cytogenetic response was obtained in 77% of dasatinib patients versus 66% of imatinib patients (p = .0001). The rate of major molecular response was 46% versus 28% for dasatinib and imatinib, respectively (p < .00001). Other notable findings include a higher rate of complete cytogenetic response for dasatinib at the 3-, 6-, and 9-month assessment periods and a lower rate of progression to accelerated or blast phase for the dasatinib arm. Both therapies were well tolerated with toxicity profiles comparable to previous trials with dasatinib and imatinib. Hematologic toxicities were similar between arms with the exception of grade 3 or 4 thrombocytopenia (21% for dasatinib versus 10% for imatinib). Fluid retention represented the most common nonhematologic toxicity for both therapies but was overall less frequent for dasatinib than for imatinib (19% versus 42%, respectively). Pleural effusions were only observed in patients receiving dasatinib, whereas gastrointestinal intolerance,

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rash, and myalgias were more common in the imatinib arm. Grade 3 or 4 hypophosphatemia was more frequent in the imatinib group compared to the dasatinib group (4% versus 21%, respectively). QTC interval changes were seen in a small number of patients. The median change in the QTC interval from baseline was 3.0 msec in the dasatinib group and 8.2 msec in the imatinib group. The authors concluded that both therapies were well tolerated, though dasatinib demonstrated a significantly higher rate of response within the first 12 months compared with imatinib.

The Evaluating Nilotinib Efficacy and Safety in Clinical Trials—Newly Diagnosed Patients (ENESTnd trial) evaluated the benefit of nilotinib versus imatinib in 846 adult patients newly diagnosed with chronic phase CML.[4] Patients were randomized in a 1:1:1 ratio to one of three arms: nilotinib 300 mg twice daily ($n = 282$), nilotinib 400 mg twice daily ($n = 281$), or imatinib 400 mg once daily ($n = 283$). Dosage escalation of the imatinib to 400 mg twice daily was allowed for those patients exhibiting a suboptimal response ($n = 45$). No significant differences were found among each arm in terms of demographics or distribution of disease burden based on Sokal risk. At the 12-month evaluation period, the nilotinib arms demonstrated significantly greater rates of major molecular response compared to the imatinib arm (44% nilotinib 300 mg, 43% nilotinib 400 mg, and 22% imatinib; $p < .001$). A similar response was observed at the 3-, 6-, and 9-month assessments. In addition, the rates of complete cytogenetic response were higher for the nilotinib arms (80% nilotinib 300 mg, 78% nilotinib 400 mg, and 65% imatinib; $p < .001$). Other observations in this trial included 11 (4%) imatinib-treated patients progressing to accelerated phase or blast crisis versus 3 (<1%) nilotinib-treated patients combined. Overall, both therapies were well tolerated with toxicity profiles comparable to previous trials of nilotinib and imatinib. Although severe toxicities were relatively uncommon, grade 3 and 4 hematologic toxicities were observed for the nilotinib 300 mg, nilotinib 400 mg, and imatinib arms as follows, respectively: neutropenia 12%, 10%, and 20%; thrombocytopenia 10%, 12%, and 9%; anemia 3%; 3%, and 5%. The rates of nonhematologic toxicities varied between therapies with gastrointestinal intolerance, edema, and muscle spasms occurring more commonly in the imatinib arm. Rash, headache, pruritus, and alopecia, as well as elevations in bilirubin, ALT, and AST were more common among nilotinib patients. The authors concluded that the significantly greater response at 12 months with both dosages of nilotinib versus imatinib could translate to improved long-term outcomes for CML patients.

The IRIS trial demonstrated that achievement of both a complete cytogenetic response and a major molecular response within the first 12 months of therapy correlated with a low risk of CML progression.[1] These surrogate markers represent the rationale for the 12-month interim analysis for the DASISION and ENESTnd trials. Despite the absence of long-term survival data, the manufacturers of dasatinib (Sprycel®, Bristol-Myers Squibb, New York, NY) and nilotinib (Tasigna®, Novarits Pharmaceuticals Corporation, East Hanover, NJ) have pursued supplemental new drug applications for newly diagnosed chronic phase CML. In June 2010 Novartis Pharmaceuticals was granted approval to modify the labeling for nilotinib (Tasigna®) as a frontline treatment for Philadelphia chromosome-positive CML.[5] Bristol-Myers Squibb was granted a priority review for dasatinib (Sprycel®) in July 2010 and is awaiting a decision from the FDA.[6]

Although previous trials identified the secondary role of nilotinib and dasatinib in CML patients with imatinib resistance or intolerance, the results described above suggest a possible frontline application of these drug products. The DASISION and ENESTnd trials have independently demonstrated improved response rates for the next generation BCR-ABL tyrosine kinase inhibitors versus imatinib in the management of newly diagnosed, treatment-naïve patients with CML. However, confirmation of long-term survival benefit is essential to truly establish a role for these agents in the newly diagnosed patient. Furthermore, data regarding the incidence and management of BCR-ABL mutations resistant to dasatinib and nilotinib are also lacking. Clinicians should carefully consider their therapy choices and the potential implications to the patient's overall success. Until data further mature, the idea of a "triple-threat" in CML therapy has not been effectively validated.

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ASCO 46TH ANNUAL MEETING UPDATES

ASCO Highlights

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The American Society of Clinical Oncology's (ASCO) 46th Annual Meeting took place in Chicago in June 2010. I've had the opportunity to attend about a dozen ASCO annual meetings, and I find them to be busy and crowded, but informative nonetheless. The size and scope do not allow one person to attend everything offered at the meeting (that might require 5–10 people). I started each day with a coffee, an apple fritter, and a shuttle bus to McCormick Place Convention Center. There were many options and tracks offered at the meeting that were filled with clinical or administrative information, but for this discussion, I will concentrate on the clinical items presented during the plenary session. These data are determined by the scientific committee to be the most worthy of "primetime" status.

One topic discussed during the sessions was the phase 3 trial (GOG 0218) of bevacizumab (B) in the primary treatment of epithelial ovarian cancer, primary peritoneal cancer, or fallopian tube cancer. This three-arm trial involves carboplatin-paclitaxel (CP) with or without maintenance bevacizumab or with bevacizumab for 1 year. Progression-free survival (PFS) was the primary endpoint. The third arm (CP x 6 cycles + B x 1yr) provided a statistically significant longer PFS, and simply adding bevacizumab to the carboplatin-paclitaxel combination did not increase PFS. There was no difference in overall survival, but crossover was allowed. Adverse effects included those that we have come to expect from bevacizumab. Look for maintenance bevacizumab to be a part of your ovarian regimens soon.

Non-small cell lung cancer (NSCLC) was the highlighted topic for two presentations. Abstract 2 compared weekly paclitaxel combined with monthly carboplatin versus single-agent therapy (gemcitabine or vinorebine) randomized in an elderly population (70–89 years old). Though grade 3–4 hematological toxicities were significantly higher in the doublet arm (54.1% versus 17.9%), the overall survival (OS) and PFS were significantly higher (10.4 versus 6.3 months, and 6.3 versus 3.2 months) for the combination therapy.

Abstract 3 introduced a new targeted drug substance, the anaplastic lymphoma kinase (ALK) inhibitor, crizotinib. It is a selective, ATP-competitive, small-molecule, orally bioavailable inhibitor of the ALK and MET/hepatocyte growth factor (HGF) receptor tyrosine kinases. Approximately 4% of NSCLC express the EML4-ALK fusion oncogenes, which crizotinib effectively inhibits. Most patients in the trial who had this mutation had never smoked or were former smokers and had adenocarcinoma histology. Any patient who had previously had therapy or who was treated for brain metastases were administered 250 mg bid. The overall response rate (ORR) was 64% and the disease control rate was 90%. The median PFS has yet to be reached in the cohort of 76 patients. The only unusual adverse effect was a mild visual disturbance characterized as light/dark accommodation. Except for a small subset population, these are very promising data.

The final plenary presentation discussed a novel therapy for melanoma, ipilimumab (ipi). This humanized monoclonal antibody blocks the CTLA-4 receptor on a T-cell, thus keeping the T-cell "activated" (the best I can explain it without pictures), producing an immunotherapy for melanoma. This randomized, double-blind, multicenter trial produced the first improvement in survival that we have seen for melanoma. The design was gp100 peptide vaccine versus vaccine + ipi or ipi alone. Median OS was 4 months greater in the ipi arms than the vaccine arm, and all other endpoints were statistically significant as well. Although 4 months might not seem overwhelming, the fact that there was an improvement in treating metastatic melanoma was worthy of plenary status. However, the benefits were not without toxicity; the most common immune-related adverse events were skin- and gastrointestinal-related, requiring corticosteroid therapy in 10%–14% of the cases. Treatment-related deaths were higher in the treatment arm as well.

This meeting did not necessarily present practice-changing data; adjuvant cetuximab for colon cancer was a negative trial, and the meta analysis of bevacizumab for use in metastatic breast cancer showed no survival advantage (prompting the FDA's recent review of this indication). However, ASCO's 46th Annual Meeting presented information on several new agents with promising early results in difficult diseases, which will hopefully make a difference in treating cancer in the future.

2010 ASCO Meeting Summary: Spotlight on Pediatrics

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Houston, TX

The 46th Annual American Society of Clinical Oncology (ASCO) Meeting had much to offer attendees interested in childhood and adolescent cancers. From educational symposia to oral abstract presentations to poster sessions, numerous pediatric oncology practitioners were at the meeting to share the latest advances in the field of pediatric cancer.

Some of the educational sessions and oral abstract sessions focused on neuroblastoma, which continues to be an area of active research. Current research efforts include identifying patients at high risk for disease relapse and further refining the exact role of vaccines as a therapeutic modality. Wendy London, PhD, of the Children's Hospital of Boston presented a recent analysis of factors that influence survival after relapse in children with neuroblastoma (Abstract 9518). Her group identified time to first relapse as an important predictor of survival, which will be significant in the future for stratifying patients in early clinical trials and identifying patient groups that are considered salvageable postrelapse. Alice Yu, MD PhD, of the University of California–San Diego reviewed data associated with the use of anti-GD2 (i.e., surface glycolipid molecule, disialoganglioside) antibodies as well as a new anti-iodiotype antibody, 1A7.

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BOARD AND COMMITTEE UPDATES

Update from the Board

Rowena (Moe) Schwartz, President

This has been a very busy year for HOPA, which is not unlike previous years for this relatively young organization. Our new management company, AMC, has provided support for our growth, and I would like to take this opportunity to acknowledge the collaborative work of AMC, the HOPA Board, and committee leadership during the transition of management companies. The success included a relatively smooth transition, maintenance of HOPA work, and continued organizational growth to better meet HOPA's membership needs.

HOPA Foundation

One of the most exciting successes of the past year is the HOPA Foundation. The idea of a HOPA foundation is not new, but because HOPA is such a young organization the focus (appropriately) has been on the development of the parent organization. Last fall, the board recognized that it was time to evaluate the potential for a foundation and established the HOPA Foundation Advisory Council. The charge of this group of members was to evaluate the feasibility of a foundation and present the board with a proposal. The advisory council worked under the leadership of Past President Jim Koeller, and presented a plan to the HOPA Board at the annual conference in New Orleans. The board has reviewed this proposal and has worked with legal counsel and AMC; I am happy to announce that we are in the process of moving forward with the establishment of the HOPA Foundation.

The following is some general information about the HOPA Foundation.

- The HOPA Foundation will be incorporated in Illinois.
- According to the proposed bylaws, "the HOPA Foundation is organized for charitable, educational, and scientific purposes." Certainly, we will work to ensure that the efforts of HOPA and the HOPA Foundation are complementary.
- The HOPA Foundation Board will have some overlap with the HOPA Board. The HOPA Foundation Board will include the past president, president, president-elect, and treasurer, in addition to three at-large foundation directors (who are not currently HOPA Board members).

We are finalizing the document for the HOPA Foundation incorporation; establishing the HOPA Foundation Board of Directors will be our next step.

On behalf of the HOPA Board, I would like to thank the members of the advisory council for their work.

Industry Relations Council Program

One recommendation from the HOPA Foundation Advisory Council was to develop an industry relations council for the HOPA Foundation. The board liked this idea so much that we decided to expand the concept. We are in the process of finalizing an Industry Relations Council Program that will encompass both HOPA and our newly forming HOPA Foundation.

The goal of the Industry Relations Council Program is to create a forum to facilitate ongoing dialogue between industry representation and the HOPA Board, the HOPA Foundation Board, and, ultimately, the membership. One purpose of this program is to work collaboratively with industry to develop and support programs that promote optimal, cost-effective care for individuals with cancer.

HOPA Website

It is time to give HOPA's website a facelift, and we have asked AMC to work with HOPA members on a redesign. The goal is to improve our current website and make it more accessible and useful to membership.

As you may have seen in your recent HOPA e-mail blast, we would like your help. Please tell us what you would like to see on a website. This website should be an information source about the organization for members and a resource for communicating any and all changes in the organization. Most importantly, it must be user friendly for even the most technology-challenged member and able to change as HOPA's needs and activities grow.

Strategic Planning for HOPA

We will be holding a 2-day retreat in Chicago, October 8–9, for strategic planning. Unfortunately, the Cubs regular season games will be finished, but we are optimistic (if a bit deluded) that there just may be some postseason games.

The strategic planning session will include HOPA members in addition to board members. The strategic planning facilitator is also conducting telephone interviews with members to help prepare for a successful retreat.

BCOP Recertification Committee

Julianna Burzynski, Chair
Ryan Bookout, Vice Chair

The Oncology Pharmacy Specialty Sessions for Board Certified Oncology Pharmacist (BCOP) recertification continuing education credit were presented at the 2010 HOPA Annual Conference in New Orleans, LA. The presented topics included "Innovations in the Management of Cervical Cancer—Prevention and Treatment" (Dayna McCauley), "Impact of Technology on Chemotherapy/Anticancer Medication Safety" (Joe Bubulo), "Updates in the Treatment and Prevention of Melanoma, Neuroblastoma, Wilms' Tumor, and Retinoblastoma, Oh My!: Traveling the Yellow Brick Road in Our Understanding of Pediatric Malignancies" (Susannah Koontz), "Radiation Oncology: Principles of Therapy and Treatment-Related Toxicity"(Sally Barbour), and "Pancreatic Cancer" (Dina Patel). If you missed the HOPA conference but are planning to attend the 2010 American College of Clinical Pharmacy (ACCP) Annual Meeting in Austin, TX, the lectures will be repeated in the "Oncology Pharmacy Specialty Sessions" Part 1 on October 19, 2010, from 1:30–4:30 pm and Part 2 on October 20, 2010, from 9 am–Noon. If you are attending the American Society of Health System Pharmacists (ASHP) Midyear Meeting in Anaheim, CA, the lectures will be repeated in the "Oncology Pharmacy Specialty Sessions Part 1" December 7, 2010, from 8–11 am and "Part 2" on December 7, 2010, from 2–5 pm. The examination for the Oncology Pharmacy Specialty Sessions for BCOP recertification credit is located on the HOPA University website (www.hopau.org). The examination and opportunity to claim BCOP recertification continuing education will be available online until December 31, 2010. Accreditation Council for Pharmacy Education credit is also provided for the Oncology Pharmacy Specialty Sessions.

The committee would like to thank the faculty of the Oncology Pharmacy Specialty Sessions who presented their lectures at the HOPA Annual Meeting for their hard work and continued dedication to the provision of BCOP continuing education credits via live presentations. The development of these presentations and BCOP recertification examination questions is both challenging

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and time consuming. We would like to thank the speakers in advance for their continued participation in the BCOP recertification process and for their upcoming presentations this fall. The BCOP recertification committee worked with ACCP and ASHP to improve the sign-in process for individuals seeking BCOP recertification continuing education credit at these meetings.

The BCOP recertification committee has already begun the process of developing the 2011 Oncology Pharmacy Specialty Sessions to be offered at the 2011 HOPA Annual Conference in Salt Lake City, UT, the 2011 ACCP Annual Meeting in Pittsburgh, PA, and the 2011 ASHP Midyear Meeting in New Orleans, LA. The speakers have been selected and are currently developing the presentations and BCOP recertification examination questions for next year. The topics include chronic lymphocytic leukemia, cardiovascular toxicity of chemotherapy, metastatic breast cancer, metastatic prostate cancer, germ cell tumors (testicular cancer), and vaccination of cancer patients for vaccine-preventable diseases. The committee will be looking for field testers for the 2011 BCOP recertification lectures early this winter. If you are interested in participating, please contact Ryan Bookout at Ryan.Bookout@moffitt.org.

Continuing Education Accreditation Committee

LeAnne Kennedy, Chair
Janet Espirito, Vice Chair

The Continuing Education Accreditation Committee has been recovering from the preparations of our annual conference and therefore hasn't had much to do this quarter. We are pleased to announce that from June 1, 2009 to May 31, 2010, HOPA awarded 10,750 hours of continuing pharmacy education, a record number in HOPA's 4 years as an accredited continuing education (CE) provider. That is a record number for us in just 4 years of being accredited. Although the annual conference may be over, there are still opportunities to obtain continuing pharmacy education through our HOPA U website. The committee will begin helping the education committee with some enduring projects from the annual conference, so watch for other educational opportunities in the future.

Education Committee

Susannah Kootz, Chair
Helen Marshall, Vice Chair

The Education Committee is off to a great start this year. To date, we've held two conference calls with our diverse members, including pharmacists located in Hawaii and the United Kingdom. We have brought everyone up to speed and are beginning work on our ongoing projects, which include creating patient education information handouts and developing oncology resource lists for education and training. We are also working with the HOPA Board to determine the future of best practices (previously annual programs have included investigational drugs, oral chemotherapy, and anticoagulation). The popular Oncology Boot Camp should be available on HOPA U in the near future. In May a CE program on cardiovascular complications of chemotherapy was added to HOPA U, and the 2010 Virtual Meeting (from HOPA's 2010 Annual Meeting) was launched in July, including sessions on controversies in care in solid and hematologic malignancies, risk evaluation and mitigation strategies, credentialing and chemotherapy preparation, and new drug updates in marketed products and investigational agents. The session on new drug updates in marketed products is available for CE credit. Be sure to check out HOPA U (www.hopau.org) if you were unable to attend the annual conference. We continue to work on new content for HOPA U, with additional programs in various stages of development. If you have ideas about educational endeavors that you feel the Education Committee should tackle, please contact our chair, Susannah Koontz.

Finance Committee

Antoinette Lavino, Chair
Caren Hughes, Vice Chair

The Finance Committee hit the ground running with a group of experienced members from last year and new additions with fresh perspectives: Antoinette Lavino (chair), Caren Hughes (vice chair), Michael Edwards, Peggy Wimmer, Christine Gegeckas, Casey Williams, Kristen Hehr, and Colleen Westendorf. A special thanks goes to all committee members for squeezing our conference calls into packed schedules.

Our ambitious agenda has been divided into two buckets: priority events that we endeavor to accomplish by the end of the calendar year and longer term issues that we have targeted for completion by the end of our term (May 2011).

Last year, the committee began a discussion of event cancellation insurance for the HOPA annual conference. We will review cancellation insurance offered to nonprofits as well as explaining how organizations similar to HOPA have decided to insure events. A second task for our committee is to review organization fees in collaboration with other committees (membership, annual conference) for appropriateness. Because members process renewals for both the annual conference and membership in March, this is another short-term task. The last short-term deliverable will be to consider a recommendation to add independent auditors to review HOPA's financial records.

By May 2011 we will have recommendations for the board regarding the organization's investment strategy. Given the financial market's doldrums last year and the ever-changing financial landscape, it is critical that we protect our members' and organization's plans with the right balance of investment growth and safety.

Finally, the committee will be involved in the board's long-term (3–5 years) planning strategy for HOPA.

Karen Nason (HOPA Executive Director) and Roz Gaerlan (HOPA Staff Accountant) have been involved in each of the Finance Committee's activities to date. We appreciate their patience as we grow throughout the year.

Finance, like all HOPA committees, is tasked with projects by the HOPA Board. We are fortunate that our board liaison, Vivian Park, is the immediate past chair of the Finance Committee. We look forward to a year of creative and thoughtful recommendations to the board that will support the financial health of our professional organization.

Legislative Affairs Committee

Scott Savage, Chair
Ali McBride, Vice Chair

The arrival of the new committee year has seen a continuation of last year's efforts to advance our association's legislative agenda and educate our membership about upcoming legislation and collaborative efforts with

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other professional organizations. Recently, our efforts have led to a committee structure allowing more individual participation via smaller task-force-driven initiatives. As of today, the committee is considering efforts related to risk evaluation and mitigation strategies, medication therapy management, safe handling of hazardous drugs, medication safety, practice model, oral chemotherapy, comparative effectiveness research, and the healthcare reform bill.

Membership Committee

Karen Smethers, Chair
Meredith Toma Moorman, Vice Chair

It has been an exciting time for the Membership Committee. With an influx of new talent and new ideas, we are expecting a great year. We have several goals for this year including

- coordinating membership renewal and discount programs with our management staff
- encouraging greater pharmacy technician participation in the organization
- collaborating with other committees to execute three surveys
- awarding an increased number of travel grants to the 2011 annual conference in Salt Lake City.

Our initial recruitment efforts have targeted the new PGY-2 oncology residents from the numerous programs across the country and board-certified oncology pharmacists who are not currently members of HOPA. Other recruitment items being investigated include shifting to an anniversary date for membership renewal, which would allow members to renew annually at their convenience, and initiating novel discount programs.

The Membership Committee is excited to serve you this year. Remember to encourage your colleagues, both pharmacists and technicians, to join HOPA.

Nominations and Awards Committee

Karen Fancher, Chair
Laura Jung, Vice Chair

We have just finished accepting nominations for the 2010–2011 HOPA Awards. Thank you to everyone who submitted a nomination—we have some difficult decisions to make. We look forward to announcing the winners at the 2011 HOPA 7th Annual Conference.

On September 15, 2010, we began accepting nominations for the next HOPA Board of Directors. Please take a moment to nominate a colleague. This year we will be electing a president-elect, secretary, and two members-at-large. **The deadline for nominations is November 1, 2010.** The following are position descriptions for each role.

President-elect serves a 3-year term (1 year as president-elect, 1 year as president, and 1 year as past president) on the HOPA Board. The HOPA member elected to this position shall

- perform the duties of the president in the president's absence
- serve as vice-chair of the board
- participate in all meetings of the board
- assist in carrying out the duties of the board to help set the strategic direction of the organization
- make plans for the implementation of programs when he or she assumes the office of president serve as a member of the HOPA Foundation Board throughout the 3-year term
- serve as the board liaison to committees as appointed by the board of directors.

The secretary serves a 2-year term. The HOPA member elected to this position shall

- review draft minutes from all board of director meetings
- assist in carrying out the duties of the board to help set the strategic direction of the organization
- along with the president, ensure the board reviews and updates the strategic plan on a regular basismay assist the president with committee appointments
- participate in all meetings of the board
- serve as the board liaison to committees as appointed by the board of directors.

An at-large member serves a 2-year term. The HOPA member elected to this position shall

- participate in all meetings of the board
- assist in carrying out the duties of the board to help set the strategic direction of the organization
- serve as board liaison to committees as appointed by the board of directors.

Nominations can be made on the HOPA website. Please contact Karen Fancher, Nominations & Awards Committee Chair, at kmfancher@ymail.com with any questions. Thank you for your support.

Professional Affairs Committee

Dan Zlott, Chair
Marjory Curry, Vice Chair

The Professional Affairs Committee has been working on a number of exciting developments.

Booth Development

The HOPA Board recently approved the purchase of a booth to be used at industry conferences. HOPA plans to exhibit the booth at the 2010 American Society of Health System Pharmacists (ASHP) Midyear Clinical Meeting and the 2011 American Pharmacists Association (APhA) Annual Meeting. The committee has selected a booth design and is currently working with HOPA staff members to finalize the graphic layout of the booth display. We are currently developing a guide for HOPA exhibitors, as well as tools to obtain feedback about the effectiveness of and ways to improve the booth. The committee will be seeking volunteers who will be attending the ASHP and APhA meetings to help staff the booth in the exhibit halls during the meetings.

Collaboration

The committee is continuing to expand HOPA's collaboration with other professional organizations, including ASHP, APhA, and the Oncology Nursing Society (ONS). We are currently working with APhA to continue offering a HOPA/APhA cosponsored oncology session at the APhA Annual Meeting. We are also working to develop a relationship with the APhA's student academy (APhA-ASP) to increase student exposure to oncology pharmacy. Last, members of the committee are approaching ONS leadership to discuss potential ideas for collaboration.

HOPA Grant Program Development

The Professional Affairs Committee is also reviewing several grant programs offered by other oncology and pharmacy associations to assess the goals of those programs, determine how the programs are structured, and, ultimately, to come up with several recommendations for the potential creation of HOPA's own grant program. We will be seeking input from various committees as we continue our work.

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Interest Groups

The committee was very pleased with the interest group topics and level of participation at the 2009 annual conference. We are working with the Program Committee to finalize topics for this year's interest groups and select moderators for the sessions.

Program Committee

Lauren Decloe, Chair
Jill Rhodes, Vice Chair

The Program Committee is hard at work planning the 2011 conference. We would like to thank the 2010 conference attendees for providing feedback on the speaker and meeting evaluations. This information is valuable as we work toward developing the educational content for the next annual conference.

New for this year, the Program and Education Committees have collaborated to bring a virtual meeting option to HOPA U. A sample of eight sessions from the 2010 conference (including one course eligible for CE credit) are available for members who were unable to attend the 2010 conference or those who wish to view favorite sessions again.

Please visit HOPA U (www.hopau.org) for these and other continuing education opportunities.

The committee is working to identify a unique and compelling keynote address to kick off the 2011 annual conference. This year's conference agenda will be similar to previous conferences and will include some minor changes to reflect comments from the 2010 evaluations. Educational programming is being developed in conjunction with other committees to provide a wide variety of offerings to meet the diverse needs of our membership.

Other initiatives for the upcoming year include

- developing a session at the annual conference to foster HOPA's relationship with international oncology pharmacy organizations and colleagues
- collaborating with the HOPA Board and other committees to create a consistent process for speaker selection and evaluations
- contributing to the HOPA budgeting process to ensure that we are fiscally responsible in our meeting planning.

The HOPA 7th Annual Conference will take place March 23–36, 2011, in Salt Lake City, UT. Please continue to visit the HOPA website to view conference updates and registration information as it becomes available.

Publications Committee

Brooke Bernhardt, Chair
Stacy Shord, Vice Chair

The Publications Committee got off to a quick start with the coordination and publication of this newsletter. In addition, members within the committee volunteered to be part of the HOTopics subcommittee. This subcommittee will gather ideas for the next webinar topic, solicit potential speakers, develop a process for the peer review of the slides, and create a standard operating procedure for the HOTopics program. Subcommittee members include Brooke Bernhardt, Niesha Griffith, Suwicha Limvorsak, Kerry Parsons, Brandy Strickland, and Stacy Shord (subcommittee chair). If you have any questions, comments, or suggestions for future newsletters or HOTopics webinars, please contact Brooke Bernhardt (mbbernha@txccc.org) or Stacy Shord (shordfamily@gmail.com).

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COMMITTEE UPDATES

Other endeavors for the committee in the upcoming year include additional quarterly newsletters and a survey of the membership regarding the status of and potential improvements to the recently updated HOPA Listserv.

The 2010–2011 Publications Committee members are Amelia Chan, Russell Crawford, Anne DeLisa, Erika Gallagher, Kelly Gregory, Jim Hart, Paul Hoffman, Suwicha Limvorsak, Man Yee Merl, Kerry Parsons, Adam Peele, Lisa Savage, Brandy Strickland, Stacy Shord (vice-chair), and Brooke Bernhardt (chair).

Research Committee

David Frame, Chair
Kellie Jones, Vice Chair

It is time to show off the HOPA talent. The Research Committee urges you to please submit projects that you have completed for poster presentation at the 2011 HOPA 7th Annual Conference. The abstracts are due on Monday, October 4. You may also submit an "encore" presentation of work that you have presented at another meeting. We know we have a lot of talent in this group, and this is a great opportunity to share that talent and network with other members. This is a valuable chance to come up with new collaborations and projects.

We would also like to remind all of the preceptors and residents that the deadline for the fellow, resident, and student abstracts is January 17, so keep working on those projects! In addition, the deadline for submitting a letter of intent for the 2011 HOPA Investigator Research Grant is September 29. This grant, which can be for as much as $50,000, will be awarded in early 2011 through a competitive peer-review process. Please see the HOPA website for details. This is a great opportunity to start developing your research ideas.

We are also happy to announce that there will be a research workshop on Wednesday, March 23, 2011, immediately before the 2011 annual conference begins. The workshop, "Accomplishing Meaningful Research in 1 Year," will be a 2-hour workshop designed to provide HOPA members with a defined framework for developing formal hypothesis-driven and descriptive research projects. The workshop will also provide guidance for research project design (e.g., setting realistic timelines, expectations, and objectives and identifying possible sources of funding). We hope to see you there!

The Research Committee is also working to enhance research communities and opportunities within HOPA. If you have pharmacy-driven projects, ongoing collaborations, or ideas to increase these endeavors, we would love to hear from you!

Standards Committee

Myke Green, Chair
Jamie Poust, Vice Chair

Now in its second year of existence, the Standards Committee has charted an exciting and ambitious agenda for 2010–2011. With a combination of new and returning members, work on the renal dosing of antineoplastics standard continues, along with developing standard operating procedures (SOPs) for the committee. The Standards Committee is also creating a task force to address investigational agents in oncology. This task force is charged with creating guidelines and SOPs for handling, distributing, returning, and accountability of investigational agents. Later this year, a survey will be sent to all HOPA members to identify HOPA members interested in and experienced with investigational agents to serve on this task force.

SUBMIT YOUR POSTER ABSTRACTS AND SHARE YOUR KNOWLEDGE AT THE 2011 HOPA ANNUAL CONFERENCE

HOPA is accepting research poster abstracts for consideration for the HOPA 2011 Annual Conference. There are two options for submitting an abstract, depending on whether you are a practitioner or a trainee (resident, student, or fellow). You must be a HOPA member to submit an abstract. At least one author must register for the 2011 Annual Conference and be present at the poster sessions. More information can be found at www.hoparx.org.

PRACTITIONER RESEARCH ABSTRACTS | Deadline for submission: Monday, October 4, 2010
TRAINEES: RESEARCH IN PROGRESS | Deadline for submission: Monday, January 17, 2011

Questions may be directed to Nichole Arroyo, education administrator, at narroyo@connect2amc.com or 847.375.4873.

DRUG UPDATES

Cabazitaxel (Jevtana®)

Class: Microtubule inhibitor, taxane
Indication: Treatment of hormone-refractory metastatic prostate cancer in combination with prednisone in patients previously treated with a docetaxel-containing regimen
Dose: 25 mg/m^2 administered as a 1-hour intravenous infusion every 3 weeks in combination with oral prednisone 10 mg daily
Premedication: Premedicate 30 minutes prior to each dose with intravenous antihistamine (diphenhydramine 25 mg or equivalent), intravenous corticosteroid (dexamethasone 8 mg or equivalent), and intravenous H_2 antagonist (ranitidine 50 mg or equivalent)
Dose modifications

- **Prolonged grade ≥ 3 neutropenia (greater than 1 week):** Delay treatment until neutrophil count > 1,500 cell/mm^3, then reduce dose of cabazitaxel to 20 mg/m^2 and use G-CSF for secondary prophylaxis.
- **Febrile neutropenia:** Delay treatment until improvement or resolution and until neutrophil count > 1,500 cells/mm^3, then reduce dose of cabazitaxel to 20 mg/m^2 and use G-CSF for secondary prophylaxis.
- **Grade ≥ 3 diarrhea:** Delay treatment until improvement or resolution, then reduce dose of cabazitaxel to 20 mg/m^2.

Common adverse effects: Anemia, abdominal pain, alopecia, anorexia, arthralgia, asthenia, back pain, constipation, cough, diarrhea, dysguesia, dyspnea, fatigue, hematuria, leukopenia, nausea, neutropenia, peripheral neuropathy, pyrexia, thrombocytopenia, and vomiting
Serious adverse effects: Hypersensitivity reactions, neutropenia, renal failure, and severe diarrhea
Drug interactions: Cabazitaxel is primarily metabolized by CYP3A4 and to a lesser extent by CYP2C8. Consider dose adjustment when concomitant therapy with CYP3A4 inhibitors and inducers is required.

Cabazitaxel in Hormone-Refractory Prostate Cancer

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Prostate cancer is the most common cancer among men, with an estimated 217,000 new cases and 32,000 deaths each year in the United States.[1] Age is the most significant risk factor for prostate cancer and the median age at diagnosis is 68 years. Prostate cancer metastasizes most commonly to pelvic lymph nodes and bones. First-line treatment options for metastatic disease include primary androgen ablation, which leads to symptomatic improvement in approximately 75% of patients.[2] The disease eventually becomes refractory to hormone therapy in all patients.

Treatment options in hormone-refractory disease include chemotherapy, radiotherapy, and palliative measures. The first-line chemotherapy regimen is docetaxel 75 mg/m^2 every 3 weeks with prednisone 10 mg daily.[3] Survival benefit with this regimen was observed in a randomized phase 3 trial in which docetaxel with prednisone 10 mg daily demonstrated significant survival benefit compared to mitoxantrone 12 mg/m^2 every 3 weeks with prednisone 10 mg daily (18.9 months versus 16.5 months, respectively).[4]

Until recently, there has been no standard of care for second-line therapy demonstrating survival benefit following first-line docetaxel. Mitoxantrone 12 mg/m^2 every 3 weeks with prednisone 10 mg daily has shown palliative benefit in patients with hormone-refractory prostate cancer.[2] Clinical trials, additional chemotherapy, and best supportive care are all reasonable second-line options as well.

Cabazitaxel, a novel taxane, has demonstrated activity in docetaxel-resistant tumors. Cabazitaxel is a microtubule inhibitor that binds to tubulin to promote assembly into microtubules and simultaneously inhibit disassembly. This action results in stabilization of microtubules and inhibition of mitotic cellular functions.[5]

Cabazitaxel received approval from the U.S. Food and Drug Administration (FDA) 11 weeks after submission for the treatment of hormone-refractory metastatic prostate cancer in combination with prednisone in patients previously treated with a docetaxel-containing regimen.

The safety and efficacy of cabazitaxel with prednisone was compared to mitoxantrone with prednisone in a randomized phase 3, multicenter trial (TROPIC).[6] Patients with metastatic hormone-refractory prostate cancer that progressed during or after a docetaxel-containing regimen were randomized to receive cabazitaxel 25 mg/m^2 every 3 weeks with prednisone 10 mg daily or mitoxantrone 12 mg/m^2 every 3 weeks with prednisone 10 mg daily for a maximum of 10 cycles. The primary endpoint was overall survival (OS) and secondary endpoints were progression-free survival (PFS), response rate, pain measures, and safety.

Seven hundred fifty-five patients were enrolled; 378 in the cabazitaxel group and 377 in the mitoxantrone group. Based on intention to treat analysis, patients receiving cabazitaxel demonstrated a statistically significantly longer OS compared to mitoxantrone (hazard ratio 0.70; 95% CI, 0.59, 0.83; $p < .0001$).[6] Median OS in the cabazitaxel group was 15.1 months compared to 12.7 months in the mitoxantrone group. Tumor response rate was 14.4% with cabazitaxel versus 4.4% with mitoxantrone ($p = .005$) and median time to progression was 8.8 months with cabazitaxel versus 5.4 months with mitoxantrone ($p < .001$). Median number of cycles was 6 with cabazitaxel compared to 4 with mitoxantrone.[6]

Side effects most commonly reported with cabazitaxel therapy include neutropenia, anemia, leukopenia, thrombocytopenia, diarrhea, fatigue, nausea, vomiting, constipation, and asthenia. The most frequent grade 3/4 toxicity was neutropenia observed in 82% of cabazitaxel patients and 58% of mitoxantrone patients. Rates of febrile neutropenia were 7.5% in the patients treated with cabazitaxel and 1.3% in the patients treated with mitoxantrone.[6] Patients older than 65 years of age are more likely to experience fatal outcomes and should be monitored closely. The most common adverse effects leading to treatment discontinuation were neutropenia and renal failure.

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Cabazitaxel therapy should be initiated at 25 mg/m^2 every 3 weeks in combination with prednisone 10 mg daily. Cabazitaxel should not be administered to patients if neutrophil counts are ≤1,500 $cells/mm^3$ or if they have a history of severe hypersensitivity to cabazitaxel or polysorbate 80. Primary prophylaxis with granulocyte colony stimulating factor (G-CSF) may be considered in patients with high-risk clinical features (age >65 years, poor performance status, previous episodes of febrile neutropenia, extensive prior radiation ports, poor nutritional status, or other serious comorbidities).[5] Dose reductions to 20 mg/m^2 should be considered in patients with prolonged grade ≥ 3 neutropenia, febrile neutropenia, and grade ≥ 3 diarrhea. Patients who experience grade ≥ 3 neutropenia or febrile neutropenia should receive secondary prophylaxis with G-CSF with their next cabazitaxel treatment. Cabazitaxel should be discontinued if patients continue to experience severe adverse reactions after a dose reduction. Dose modifications may also be necessary in patients who receive concomitant treatment with strong CYP3A4 inhibitors and inducers, although formal drug interaction trials have not been conducted.[5]

Cases of renal failure have been reported with cabazitaxel and should be managed aggressively. Caution should be used in patients with severe renal impairment (CrCl < 30 mL/min). Patients with hepatic impairment (total bilirubin ≥ ULN, or AST and/or ALT ≥ 1.5 x ULN) were excluded from the randomized clinical trial and impaired hepatic function is likely to increase cabazitaxel concentrations. Cabazitaxel should not be used in patients with hepatic impairment.[5]

Additional clinical considerations for cabazitaxel therapy include the administration of appropriate premedications. Severe hypersensitivity reactions can occur and may include generalized rash and erythema, hypotension, and bronchospasm. Patients should receive an intravenous antihistamine, corticosteroid, and H_2 antagonist 30 minutes prior to the chemotherapy infusion to prevent hypersensitivity reactions. Antiemetic prophylaxis is recommended as needed[5].

Cabazitaxel is available as a single-use vial 60 mg/1.5 mL and is supplied with 5.7 mL of diluent. Cabazitaxel is formulated with polysorbate 80. The single-use vial requires two dilutions prior to administration and should not be compounded or administered using PVC infusion containers and polyurethane infusion sets[5].

Based on the available literature, cabazitaxel has shown positive results in metastatic hormone-refractory prostate cancer patients. It received expedited approval from the FDA as a second-line chemotherapy option for patients previously treated with docetaxel-containing regimens. The approval of cabazitaxel was based on a randomized phase 3, multicenter trial of 755 patients. The trial supported that cabazitaxel with prednisone yielded a 2.3 month survival benefit over mitoxantrone with prednisone.[6] In conclusion, cabazitaxel is a promising chemotherapy treatment option for patients with hormone-refractory prostate cancer. Further studies comparing overall survival between cabazitaxel with prednisone and docetaxel with prednisone should be conducted to evaluate the efficacy of this novel taxane.

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DRUG UPDATES

Sipuleucel-T (Provenge®)

Class: CD54+ autologous cellular immunotherapy
Indication: Asymptomatic, or minimally symptomatic metastatic castrate-resistant (hormone refractory) prostate cancer
Dose: Three doses administered as an IV infusion, 2 weeks apart
Common adverse events: Back pain, chills, fatigue, fever, headache, joint ache, nausea
Adverse event prevention: Premedicate with acetaminophen and diphenhydramine 30 minutes before administration.
Drug Interactions: No formal drug-drug interactions have been observed with sipuleucel-T. Concomitant use with chemotherapy and immunosuppressives has not been studied.

Provenge® (Sipuleucel-T) in Metastatic Castrate-Resistant (Hormone Refractory) Prostate Cancer

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Prostate cancer is the second leading cause of cancer death in men in the United States, accounting for approximately 32,000 deaths per year. Current treatment options include radiation, surgery, and medical castration with luteinizing hormone releasing hormone (LHRH) agonists/antagonists.[1] Initial hormonal treatments, targeted at decreasing testosterone levels to below 50 ng/dl, demonstrate response rates of up to 80%, but most men will present with recurrence in 2–4 years. Patients who recur despite castration-level testosterone are classified as androgen independent (AIPC) or hormone refractory. Modest survival benefits have been derived from docetaxel-based chemotherapy in AIPC. However, grade 3 and 4 toxicities (anemia, neutropenia, neuropathies) preclude this regimen from being acceptable for all patients.[2] New agents to treat AIPC are clearly needed.

Sipuleucel-T was approved by the U.S. Federal Food and Drug Administration (FDA) on April 29, 2010, for asymptomatic or minimally symptomatic AIPC. Sipuleucel-T is an autologous cellular immunotherapy product produced by culturing a patient's antigen-presenting cells (APCs) with a recombinant fusion protein of prostatic acid phosphatase (PAP) linked to granulocyte-macrophage colony-stimulating factor (GM-CSF). PAP is known to be present in 95% of prostate cancers.[2]

Phase 1 and 2 trials of sipuleucel-T in hormone-refractory prostate cancer reported decreases of PSA by 50% or greater in 10% of patients studied. Immune responses were demonstrated in early studies by both T-cell stimulation and reductions in PAP. A delay in time to progression (TTP) was seen in those patients who had immune response to sipuleucel-T. Adverse effects included chills, fatigue, fever, myalgia, and pain.[3]

A larger phase 3 trial was conducted in patients with metastatic, asymptomatic hormone-refractory prostate cancer (Study D9901).[5] Patients were randomized in a 2:1 fashion to receive either three infusions of sipuleucel-T or placebo over 30 minutes at weeks 0, 2, and 4.

Nineteen centers enrolled 127 patients. All patients had histologically confirmed adenocarcinoma of the prostate, radiologic evidence of metastases, castration level serum testosterone, and a life expectancy of greater than 3 months. Patients were excluded for electrocorticography (ECOG) performance status greater than 1; cancer-related bone pain; opioid for cancer pain; visceral metastases; or inadequate hematologic, renal, or hepatic function. Patients were continued on LHRH agonist therapy and bisphosphonate therapy if initiated at least 30 days prior to registration. All other treatment-related therapy had to be concluded at least 1 month prior to the trial, including radiation, investigational agents, and saw palmetto. Previous chemotherapy had to be completed 6 months prior to a patient's enrollment in the study or 3 months prior if the patient demonstrated a CD4+ T-cell count greater than 400.[3]

Patients underwent leukaphoresis, and the final autologous product was administered within approximately 48 hours. All patients were premedicated with acetaminophen and diphenhydramine. Grade 1 and 2 toxicities were seen in both the sipuleucel-T (70.7%) and control (68.9%) groups. Toxicities included rigors, fever, fatigue, arthralgia, and dyspnea.

The primary endpoint in the trial TTP was not statistically significant. The median TTP was 11.7 weeks in the active arm versus 10.0 weeks for placebo. Although the study was not statistically powered to detect differences in survival, all patients were followed for survival up to 36 months. The median overall survival (OS) was 25.9 months in patients receiving sipuleucel-T versus 21.4 months for placebo.[4]

An identical trial (D9902A) was suspended early based on TTP results in D9901. An integrated analysis of the two studies was performed to evaluate treatment effects on the combined patient population. An increase in cardiovascular events was observed in the treatment arm (7.5%) versus control (2.6%).[4]

FDA approval was granted based on a double-blind, multicenter phase 3 trial that enrolled 512 patients randomized in a 2:1 ratio to sipuleucel-T or placebo.[5] Patients received leukaphoresis, which was followed 3 days later by study drug infusion at weeks 0, 2, and 4. Patients were included if they had documented metastases, were asymptomatic, and had serum testosterone levels less than 50 ng/dl. Patients with brain, liver, or lung metastases were excluded, as were as those on opioids for moderate to severe pain. The primary end point was OS. Median survival was 25.8 months on sipuleucel-T versus 21.7 months on placebo. Toxicities were generally mild to moderate and similar to those observed in the D9901/D9902A phase III trials.[5]

Sipuleucel-T (Provenge®) is available as a patient-specific infusion bag. At a minimum, it includes 50 million autologous CD54+ cells activated with a recombinant human protein consisting of prostatic acid phosphatase linked to PAP-GM-CSF. It is suspended in 250 mL of lactated Ringer's solution. It is intended solely for autologous use. Treatment with oral acetaminophen and diphenydramine is recommended 30 minutes prior to sipuleucel-T (Provenge®) administration to decrease the infusion-related adverse events. The infusion should

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be retained in the polyurethane container until the time of administration. The autologous preparation should be infused intravenously over 60 minutes and should not be used with a cell filter. Treatment with sipuleucel-T consists of three total infusions with 2-week intervals separating them.[6]

Sipuleucel-T improves OS by approximately 4 months in asymptomatic or minimally symptomatic AIPC. No difference was observed in clinical trials in TTP versus placebo. The overall toxicity profile is mild to moderate and the infusion is well tolerated. Ninety-five percent (95%) of study participants received all three infusions. Patients with cardiac or pulmonary conditions should be monitored closely. The cost of treatment ranges from $15,000–$20,000 per infusion. The Centers for Medicare & Medicaid is currently reviewing reimbursement for sipuleucel-T. A final decision is expected in early 2011.

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ASCO 46TH ANNUAL MEETING UPDATES

2010 ASCO Meeting Summary: Spotlight on Pediatrics

continued from page 3

Although most people view the ASCO meeting as a forum for discussing solid tumors, there were notable studies presented this year that focused on patients with hematological malignancies. One of the most discussed oral abstract presentations was delivered by Steven Lipshultz, MD, from the University of Miami (Abstract 9513). Dr. Lipshultz and his colleagues analyzed children treated for acute lymphoblastic leukemia (ALL) with doxorubicin administered either as a bolus dose or as a continuous infusion over 48 hours according to the DFCI Protocol 91-01. Progressive cardiac dysfunction as measured by serial echocardiographic parameters was noted in both arms, prompting the authors to conclude that length of doxorubicin infusion did not influence cardiotoxicity, as previously postulated, and alternative cardioprotective strategies in children should be investigated. Another leukemia topic of note focuses on genomic research in the setting of ALL. Laura Hogan, MD, from the New York University Medical School and her collaborators are characterizing RNA sequencing from bone marrow samples of patients with relapsed ALL to identify novel mutations that might explain chemoresistance and serve as potential drug targets in the future (Abstract 9521). The significance of Dr. Hogan's work was recognized by ASCO executives and earned her the 2010 Brigid Leventhal Merit Award for being the highest ranked abstract submitted in the field of pediatric oncology.

New this year was the widely anticipated "Trials in Progress Poster Session," a gathering of open, ongoing clinical trials aimed at increasing awareness of currently available research studies that foster exchange of ideas among investigators (no data or results were to be presented). Pediatric studies were showcased during this session including a phase 1 trial examining the combination of clofarabine and liposomal daunorubicin in childhood and adolescent acute myelogenous leukemia (Abstract TPS327) and a phase 2 trial evaluating the utility of bevacizumab added to standard chemotherapy regimens in the setting of childhood and adolescent patients presenting with metastatic rhabdomyosarcoma and non-rhabdomyosarcoma soft tissue sarcoma (Abstract TPS330).