Increased Incidence of Recurrent Venous Thromboembolism in Patients with Cancer Receiving Bevacizumab

Tanis L. Welch, PharmD; Sarah M. Gressett Ussery, PharmD, BCOP; Kevin C. Kelly, PharmD, BCPS; Jonathan E. Dowell, MD; Sachin R. Shah, PharmD, BCOP, FCCP

Background: Venous thromboembolism (VTE) is a major cause of morbidity and mortality in patients with cancer. Bevacizumab is approved for the treatment of several types of cancer. Although VTE has been documented with the use of bevacizumab, it remains controversial whether the drug itself contributes to increased VTE risk, or if specific patient characteristics such as acquired or congenital risk factors, increase the patients’ risk for venous thrombosis.

Objective: The primary purpose of this study was to evaluate the risk of VTE in patients with a history of VTE who were receiving chemotherapy with or without bevacizumab.

Methods: Patients with documented advanced or metastatic colorectal cancer (CRC) or non–small-cell lung cancer (NSCLC) who received chemotherapy between January 2002 and September 2011 were retrospectively reviewed. Data were collected for patients who met the inclusion criteria, including age ≥18 years, advanced or metastatic CRC or NSCLC treated with first-line combination chemotherapy, and an Eastern Cooperative Oncology Group performance status of 0 to 2. Patients aged ≥89 years or who had received previous vascular endothelial growth factor inhibitor treatment were excluded from the analysis.

Results: A total of 209 patients met the inclusion criteria. Of these, 173 patients without a history of VTE received bevacizumab therapy, 13 patients with a history of VTE received bevacizumab therapy, and 23 patients who had a history of VTE received chemotherapy alone. Overall, 60.8% of patients had CRC and 39.2% had NSCLC. Patients with a history of VTE who received bevacizumab had a significantly higher incidence of VTE compared with patients without a history of VTE (23.1% vs 5.2%, respectively; \( P = 0.040 \)). In addition, the incidence of recurrent VTE was higher in patients receiving bevacizumab compared with patients receiving chemotherapy alone (23.1% vs 8.7%, respectively; \( P = 0.328 \)).

Conclusion: The use of bevacizumab in patients with a history of VTE may be associated with increased risk for a subsequent VTE.
clonal antibody, neutralizes VEGF, thereby preventing VEGF from binding to its receptor and subsequently inhibiting the angiogenic process.4

Bevacizumab has been approved for, and has been shown to be effective in, the treatment of advanced or metastatic colorectal cancer (CRC), advanced or metastatic non–small-cell lung cancer (NSCLC), glioblastoma, and renal-cell carcinoma.5,8 Several unique and severe adverse effects are associated with the use of bevacizumab, including, but not limited to, hypertensive crisis, nephritic syndrome, gastrointestinal tract perforation, wound dehiscence, hemorrhage, arterial thromboembolic events, neutropenia, infection, and congestive heart failure.4,9 Although venous thromboembolism (VTE) has been documented with the use of bevacizumab, it remains controversial whether the drug itself contributes to increased risk for VTE or if specific patient characteristics, such as acquired or congenital risk factors, increase the patients’ risk for venous thrombosis.10,11

VTE is a major cause of morbidity and mortality in patients with cancer. The etiologies of VTE in cancer include the inherent hypercoagulable state, vessel wall trauma, and vessel stasis.1 The frequency of cancer-associated VTE is increased further by the presence of additional risk factors, such as acquired or congenital thrombophilia, prolonged immobilization, surgical procedures, cancer type and disease burden, chemotherapy regimen and duration, comorbid conditions, and concomitant medications. It has been reported that VTE increases the likelihood of death by 2- to 8-fold in patients with cancer.12

The overall incidence of VTE in patients with metastatic or advanced CRC or NSCLC who receive treatment with bevacizumab varies considerably among phase 2 and 3 randomized controlled trials (RCTs; range, 3%-17.6%).13-16 To date, there have been 2 meta-analyses examining the incidence of VTE in patients treated with chemotherapy plus bevacizumab. However, the conclusions of these 2 studies are conflicting. Nalluri and colleagues determined that patients treated with bevacizumab had a significantly increased risk of VTE, relative risk of 1.33 (95% confidence interval [CI], 1.13-1.56; P <.001) compared with the risk in the control groups.10 Alternatively, Hurwitz and colleagues concluded that there was no significant increased risk for VTE in patients receiving bevacizumab versus controls (odds ratio, 1.14; 95% CI, 0.96-1.35; P = .13).11

Because of the conflicting results of these meta-analyses, a wide variation in results in previous RCTs, and limited current literature, it is uncertain whether the addition of bevacizumab to chemotherapy increases patients’ risk for VTE. Furthermore, there are no studies directly evaluating the risk for recurrent VTE in patients with a history of VTE who are treated with bevacizumab. In clinical practice, a history of VTE has typically not precluded the use of bevacizumab in patients with cancer.

The purpose of this study is to evaluate the risk for recurrent VTE in patients receiving chemotherapy plus bevacizumab.

Methods

This retrospective cohort chart review included patient data from January 1, 2002, through September 30, 2011. Patients were eligible for inclusion if they were aged ≥18 years, had an Eastern Cooperative Oncology Group (ECOG) performance status of ≤2, and had a diagnosis of advanced or metastatic CRC or NSCLC and were receiving first-line combination chemotherapy. Patients with previous VEGF inhibitor treatment were excluded.

Patients were identified with the use of International Classification of Diseases, Ninth Revision (ICD-9) codes for NSCLC (162.00) and CRC (153.00). Demographic information collected included age, sex, body mass index (BMI), and baseline ECOG performance status. Risk factors at baseline were also collected, including VTE history and location; baseline medication history, including hormonal therapy; erythropoietin stimulating agents; or megesterol. In addition, medical history of congestive heart failure, myocardial infarction or cerebrovascular accident, platelets ≥350,000, and major or minor surgery within 30 days or while receiving treatment were recorded.

Surgery was defined as major if the surgery lasted at least 1 hour with anesthesia and/or surgery with extensive tissue injury (ie, abdominal, thoracic, or orthopedic surgery, or reconstructive plastic surgery). Minor surgery was defined as a procedure lasting <1 hour.17 In addition, baseline use of anticoagulants or antiplatelets, cancer diagnosis, use of a chemotherapy regimen (initiation date and discontinuation date), dose of bevacizumab (if included in a regimen), total number of chemotherapy cycles received, and incidence and location of VTE while receiving treatment and up to 60 days after discontinuation of treatment were collected. The incidence of VTE was further delineated as inpatient or outpatient; inpatient was defined as a patient being admitted to the hospital for ≥3 days and outpatient for ≤3 days.

Computerized progress notes, pharmacy records, and imaging reports were reviewed. The study was conducted in compliance with the Institutional Review Board and the research and development committee of the Veterans Affairs North Texas Health Care System and Texas Tech University Health Sciences Center.
The primary objective of the study was to evaluate the incidence of recurrent VTE in patients receiving bevacizumab. In addition, the incidence of recurrent VTE in patients receiving chemotherapy without bevacizumab exposure and primary incidence of VTE in patients receiving bevacizumab were evaluated and compared with the primary objective. Group comparison for categorical variables was performed using chi-square or Fisher exact test. Mann-Whitney U test was used to evaluate continuous variables. A multivariate regression model was used to test the relationship between the incidence of VTE and potential confounding factors. All data were analyzed using the Minitab 15 Statistical Software (State College, PA). Statistical significance was defined as \( P \leq 0.05 \).

**Results**

A total of 1422 patients were initially identified using ICD-9 codes for CRC and NSCLC; of these, 1213 patients were excluded. Of the 209 patients who met the inclusion criteria, 186 patients were treated with chemotherapy plus bevacizumab. Of those 186 patients, 173 had no history of VTE (Group A) and 13 had a history of VTE (Group B). The third group, considered the control group (Group C), included 23 patients with a history of VTE who were treated with chemotherapy, without bevacizumab. Overall, 60.8% of patients had CRC and 39.2% had NSCLC.

Baseline characteristics are reported in Table 1. There were no significant differences in baseline characteristics among all 3 groups. The mean age was 62 years, and the

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Patients' Baseline Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Bevacizumab</td>
</tr>
<tr>
<td></td>
<td>No VTE history</td>
</tr>
<tr>
<td></td>
<td>Group A (N = 173)</td>
</tr>
<tr>
<td>Age, mean yrs (± SD)</td>
<td>62.5 (± 8.5)</td>
</tr>
<tr>
<td>Male, N (%)</td>
<td>171 (99)</td>
</tr>
<tr>
<td>BMI ≥25 kg/m², N (%)</td>
<td>96 (55)</td>
</tr>
<tr>
<td>ECOG performance status, N (%)</td>
<td>48 (28)</td>
</tr>
<tr>
<td>0</td>
<td>87 (50)</td>
</tr>
<tr>
<td>1</td>
<td>38 (22)</td>
</tr>
<tr>
<td>Tumor site</td>
<td></td>
</tr>
<tr>
<td>CRC, N (%)</td>
<td>113 (65)</td>
</tr>
<tr>
<td>NSCLC, N (%)</td>
<td>60 (35)</td>
</tr>
<tr>
<td>History of VTE</td>
<td></td>
</tr>
</tbody>
</table>
| Lower DVT, N (%) | NA | 6 (46) | 11 (48)

| PE, N (%) | NA | 4 (31) | 7 (30) |
| Other (ie, mesenteric vein, splenic vein, superior vena cava, brachiocephalic, portal vein), N (%) | NA | — | 4 (17) |
| Concurrent anticoagulation, N (%) | 9 (69) | | 13 (57)

| Warfarin, N (%) | 4 (100) | 4 (44) | 6 (46) |
| LMWH, N (%) | NA | 5 (36) | 8 (61) |

**NOTE**: None of these data were statistically significant.

*One patient had both lower DVT and PE.

*One patient was on both warfarin and LMWH.

BMI indicates body mass index; CRC, colorectal cancer; DVT, deep vein thrombosis; ECOG, Eastern Cooperative Oncology Group; LMWH, low-molecular-weight heparin; NA, not applicable; NSCLC, non–small-cell lung cancer; PE, pulmonary embolism; SD, standard deviation; VTE, venous thromboembolism.
## Table 2: Patients' VTE Risk Factors at Baseline

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Bevacizumab</th>
<th>No VTE history Group A (N = 173)</th>
<th>VTE history Group B (N = 13)</th>
<th>VTE history Group C (N = 23)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHF, N (%)</td>
<td></td>
<td>3 (2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Previous CVA, N (%)</td>
<td></td>
<td>6 (3)</td>
<td>1 (8)</td>
<td>3 (13)</td>
</tr>
<tr>
<td>Previous MI, N (%)</td>
<td></td>
<td>14 (8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ESA, N (%)</td>
<td></td>
<td>22 (13)</td>
<td>2 (15)</td>
<td>2 (9)</td>
</tr>
<tr>
<td>Hormonal therapy, N (%)</td>
<td></td>
<td>1 (1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acquired/congenital thrombophilia</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Megesterol, N (%)</td>
<td></td>
<td>28 (16)</td>
<td>1 (8)</td>
<td>4 (17)</td>
</tr>
<tr>
<td>Platelets ≥350,000, N (%)</td>
<td></td>
<td>40 (23)</td>
<td>3 (23)</td>
<td>4 (17)</td>
</tr>
<tr>
<td>Surgery within 30 days of, or while receiving treatment, N (%)</td>
<td></td>
<td>22 (13)</td>
<td>3 (23)</td>
<td>2 (9)</td>
</tr>
<tr>
<td>Major, N (%)</td>
<td></td>
<td>3 (14)</td>
<td>1 (33)</td>
<td>1 (50)</td>
</tr>
<tr>
<td>Minor, N (%)</td>
<td></td>
<td>19 (86)</td>
<td>2 (67)</td>
<td>1 (50)</td>
</tr>
</tbody>
</table>

CHF indicates congestive heart failure; CVA, cerebrovascular accident; ESA, erythropoietin-stimulating agent; MI, myocardial infarction; VTE, venous thromboembolism.

## Table 3: Chemotherapy Characteristics

<table>
<thead>
<tr>
<th>Treatment regimen</th>
<th>Chemotherapy plus bevacizumab</th>
<th>Chemotherapy and no bevacizumab</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No VTE history Group A (N = 173)</td>
<td>VTE history Group B (N = 13)</td>
</tr>
<tr>
<td>Dose of bevacizumab, N (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 mg/kg</td>
<td>48 (28)</td>
<td>6 (46)</td>
</tr>
<tr>
<td>7.5 mg/kg</td>
<td>70 (40)</td>
<td>3 (23)</td>
</tr>
<tr>
<td>15 mg/kg</td>
<td>55 (32)</td>
<td>4 (31)</td>
</tr>
<tr>
<td>Weeks on treatment, median</td>
<td>17.7</td>
<td>15.7</td>
</tr>
<tr>
<td>Number of cycles, mean (± SD)</td>
<td>6.8 (± 5.7)</td>
<td>7.6 (± 5.7)</td>
</tr>
<tr>
<td>Regimen, N (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FOLFOX/XELOX</td>
<td>78 (45)</td>
<td>7 (54)</td>
</tr>
<tr>
<td>FOLFIRI/XELIRI</td>
<td>13 (8)</td>
<td>1 (8)</td>
</tr>
<tr>
<td>IFL</td>
<td>23 (13)</td>
<td>1 (8)</td>
</tr>
<tr>
<td>Platinum doublet&lt;sup&gt;b&lt;/sup&gt;</td>
<td>55 (32)</td>
<td>4 (31)</td>
</tr>
<tr>
<td>Other&lt;sup&gt;c&lt;/sup&gt;</td>
<td>4 (2)</td>
<td>—</td>
</tr>
</tbody>
</table>

<sup>a</sup>P = .0297.
<sup>b</sup>Platinum doublet = carboplatin/gemcitabine, carboplatin/docetaxel, carboplatin/paclitaxel, cisplatin/pemetrexed.
<sup>c</sup>Other = docetaxel alone, capicitabine alone, fluorouracil/leucovorin (5-FU/LV).

FOLFOX indicates fluorouracil/leucovorin/irinotecan; FOLFIRI, fluorouracil/leucovorin/irinotecan; FOLFOX, fluorouracil/leucovorin/oxaliplatin; IFL, irinotecan/5-fluorouracil/leucovorin; NA, not applicable; SD, standard deviation; VTE, venous thromboembolism; XELIRI, capicitabine/irinotecan; XELOX, capicitabine/oxaliplatin.
The majority of the patients were male (98%). The majority of the patients in the bevacizumab-treated groups (Groups A and B) were overweight, with a BMI of ≥25 kg/m² compared with those in Group C. The majority of patients in Groups A and B had an ECOG performance status of 1 (50% and 54%, respectively) compared with patients in Group C; 52% of these patients had an ECOG performance status of 2.

In Groups A and B, CRC was more common (65% and 62%, respectively) compared with Group C, in which NSCLC was more common (74%). Considering the 2 groups with a history of VTE (Groups B and C), the most common type of VTE was lower extremity deep vein thrombosis (DVT). These patients were most often treated with a low-molecular-weight heparin (LMWH) and 1 patient in Group C was treated with LMWH and warfarin at baseline.

Table 2 reports the VTE risk factors at baseline among the study groups. Very few patients in any of the groups had surgery 30 days before or while receiving treatment. A total of 22 patients had minor surgeries, including mediport placement (19), cystoscopy (2), and incision and drainage (1); 5 patients had major surgeries, including exploratory laparotomy (2), hemicolectomy (2), and lower abdominal resection (1). Several patients had additional VTE risk factors at baseline; however, a multivariate analysis revealed no significant difference between the bevacizumab-treated and the control group on the effect of these risk factors.

Considering the chemotherapy characteristics, specifically in the bevacizumab-receiving groups, Group A most often (40.5%) received the 7.5-mg/kg dose compared with Group B, in which the most common (46%) dose was the 5-mg/kg dose. Additional chemotherapy characteristics are listed in Table 3.

The patients in Group C received the shortest duration of treatment and subsequently the fewest number of chemotherapy cycles compared with the bevacizumab-treated groups. This difference was significant when comparing the median weeks of treatment between patients in Group B and patients in Group C—15.7 weeks versus 9.4 weeks, respectively (P = .0297).

The most common combination chemotherapy regimen used in all 3 groups was the platinum-based regimens (ie, FOLFOX [fluorouracil, leucovorin, and oxaliplatin], XELOX [capecitabine and oxaliplatin], and platinum doublets).

### Table 4: Incidence of Venous Thromboembolism, by Group

<table>
<thead>
<tr>
<th>VTE Incidence</th>
<th>Chemotherapy plus bevacizumab</th>
<th>Chemotherapy and no bevacizumab</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No VTE history Group A (N = 173)</td>
<td>VTE history Group B (N = 13)</td>
</tr>
<tr>
<td>VTE while receiving treatment, N (%)</td>
<td>9 (5.2)*</td>
<td>3 (23.1)*</td>
</tr>
<tr>
<td>Type of VTE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lower DVT, N (%)</td>
<td>3 (1.7)</td>
<td>1 (7.6)*</td>
</tr>
<tr>
<td>Upper DVT, N (%)</td>
<td>2 (1.2)</td>
<td></td>
</tr>
<tr>
<td>PE, N (%)</td>
<td>4 (2.3)</td>
<td>3 (23.1)*</td>
</tr>
<tr>
<td>Outpatient VTE, N (%)</td>
<td>9 (100)</td>
<td>2 (66.7)</td>
</tr>
<tr>
<td>Inpatient VTE, N (%)</td>
<td>—</td>
<td>1 (33.3)</td>
</tr>
</tbody>
</table>

*p = .040.

DVT indicates deep vein thrombosis; PE, pulmonary embolism; VTE, venous thromboembolism.
Among the patients treated with bevacizumab, the incidence of VTE was 5.2% (9 of 173 patients) for Group A versus 23.1% (3 of 13) for Group B ($P = .040$). The incidence was still higher in Group B compared with patients in Group C—23.1% versus 8.7% (2 of 23), respectively; however, this was not significant ($P = .328$; Figure).

The most common on-treatment VTE manifestation among Groups A and B was pulmonary embolism (PE); in Group C, an equal number of patients had lower DVT and PE. One patient in Group B and 1 in Group C had both a PE and lower DVT. All the on-treatment VTE cases were in the outpatient setting, with the exception of 1 patient in Group B who was classified as inpatient. The incidence of VTE is summarized in Table 4.

Discussion

In patients with cancer, VTE can diminish quality of life and can even result in death. VTE has been reported in patients receiving bevacizumab. We used 2 different comparator groups to better understand the clinical impact of bevacizumab therapy on the incidence of recurrent VTE. The first group (Group A) included patients without a history of VTE who received bevacizumab. This group provided a baseline for the incidence of VTE in patients receiving bevacizumab.

The comparator group (Group C) was comprised of patients with a history of VTE who received chemotherapy but not bevacizumab. This group provided the baseline risk for recurrent VTE in patients receiving chemotherapy only.

This study used a cutoff period of 60 days to consider at least 3 half-lives of bevacizumab to account for any residual effects of the drug. Our study suggests that the risk for VTE was significantly higher in patients with a history of VTE compared with patients without a history of VTE who were receiving bevacizumab. Furthermore, the risk for VTE remains high, although not significantly, even when compared with the patients with a history of VTE who were receiving chemotherapy without bevacizumab.

Overall, 69% of patients were receiving active anticoagulation therapy while taking bevacizumab. Our study suggests that there is a consistent increased risk for recurrent VTE in patients receiving bevacizumab. All 3 patients who had recurrent VTE while receiving bevacizumab were also taking therapeutically targeted anticoagulation agents.

We did not detect any significant differences between the group demographics at baseline. However, variations in ECOG performance status and types of cancers were observed between Groups B and C. The majority of the patients in Groups A and B had a performance status $<1$, whereas the majority of patients in Group C had performance status 2. In addition, 62% of the patients in Groups A and B had CRC compared with 26% in Group C. Based on these differences of ECOG performance status and cancer type distributions at baseline between the 2 groups (ie, bevacizumab-treated vs no bevacizumab), patients in Group C should have had a higher incidence of VTE. According to the VTE predictive model, patients with lung cancer are at 50% increased risk of having VTE compared with those with CRC.18

No significant difference was noted among the 3 groups regarding the VTE risk factors at baseline (Table 2). There was a higher percentage (23%) of patients with recent surgery in Group B, but the majority of the surgeries were minor. In addition, the surgeries reported occurred within 30 days of chemotherapy or chemotherapy plus bevacizumab administration and did not occur before the incidence of VTE. Patients in Group B had significantly longer duration of cancer treatment (15.7 vs 9.4 weeks; $P = .0297$) compared with Group C. This difference could be explained by the cancer type distribution and chemotherapy regimen administered in these 2 groups. The majority of patients in Group C had NSCLC and received platinum-based chemotherapy. A typical patient with NSCLC might have received 4 cycles of platinum-based chemotherapy and then might have been followed for observation. By contrast, a typical patient with CRC might have received 5-fluorouracil–based chemotherapy until the progression of cancer.

The increase in incidence of VTE in patients treated with bevacizumab may be attributed to the anti-VEGF mechanism of bevacizumab. Our study revealed a 5.2% incidence of primary VTE in patients with CRC or NSCLC who were treated with bevacizumab (Group A), which is consistent with what is reported in previous studies (incidence range, 3%-17.6%).13-16

The risk for VTE was significantly higher when bevacizumab was administered to patients with a history of VTE (23.1%) in our study compared with those without a history of VTE (5.2%). In addition, the risk for recurrent VTE was higher in patients receiving chemotherapy plus bevacizumab compared with chemotherapy alone (23.1% vs 8.7%; $P = .328$).

These results are consistent with the results of a 4-arm prospective RCT by Saltz and colleagues that included 1401 patients with metastatic CRC, in which the incidence of primary VTE was 13.5% in the bevacizumab arms.4,5 Among the 116 patients treated with anticoagulation after an initial VTE (73 in the bevacizumab plus chemotherapy arms and 43 in the chemotherapy-alone arms), the bevacizumab arms had
higher incidence of recurrent VTE compared with the control arms (31.5% vs 25.6%, respectively).4

Another pivotal first-line trial in patients with metastatic CRC (AVF2107g) evaluated the incidence of recurrent VTE in patients receiving bolus IFL (irinotecan, 5-fluorouracil, and leucovorin) with or without bevacizumab.4,19 In this trial, patients with an incidence of primary VTE received full-dose warfarin therapy. The recurrent VTE occurred in 21% (11 of 53 patients) of patients receiving bolus IFL plus bevacizumab compared with 3% (1 of 30 patients) of patients receiving bolus IFL alone.4 The key difference between these 2 trials and this present study is that these 2 trials did not evaluate the incidence of recurrent VTE in patients without previous exposure to bevacizumab.

Limitations

This study has limitations that should be considered when interpreting the results. First, the results of this study are primarily applicable to male patients with cancer, because 98% of the patients were males. Another limitation was the relatively small sample size, which might have contributed to the nonstatistical differences between the groups at baseline, and for the VTE outcomes.

Conclusion

Regardless of the study limitations, this study evaluates an important question, which to our knowledge has not been investigated, that is, the risk of recurrent VTE in patients receiving bevacizumab.

The results of this study suggest that patients with CRC or NSCLC who are receiving bevacizumab are at increased risk for recurrent VTE. This risk may be higher compared with patients receiving chemotherapy without bevacizumab. There are many clinical questions that cannot be answered by the available literature, such as the optimal timing of bevacizumab initiation after a VTE, whether the risk of VTE can be mitigated by appropriate anticoagulation, or if there is a difference in risk of recurrent VTE if patients have a provoked versus an unprovoked VTE. These are questions that still need to be answered to make concrete recommendations in the use of bevacizumab in the setting of a previous VTE. In practice, careful evaluation of risk versus benefit with the use of bevacizumab-based therapy should be considered in the setting of limited literature evaluating the risk of recurrent VTE.

Author Disclosure Statement

Dr Gressett Ussery is an employee of Celgene Corporation; Dr Dowell has received research support from Verastem and MedImmune; Dr Welch, Dr Kelly, and Dr Shah reported no conflicts of interest.

References

A 2-day congress dedicated to informing, educating, and fostering the exchange of clinically relevant information in the field of cutaneous malignancies on topics in melanoma, basal cell carcinoma, squamous cell carcinoma, Merkel cell carcinoma, and cutaneous T-cell lymphoma.

**EDUCATIONAL OBJECTIVES**

After completing this activity, the participant should be better able to:

- Review the molecular biology and pathogenesis of malignant melanoma, CTCL, BCC, and MCC, including how they relate to targeted therapy
- Describe how to tailor therapeutic options and optimal sequencing for individual patients with melanoma, CTCL, BCC, and MCC
- Utilize emerging data and recent advances with new molecular targets for the treatment of patients with metastatic melanoma, CTCL, BCC, and MCC
- Identify new technologies for the prevention and early detection of cutaneous malignancies

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Event staff will be glad to assist you with any special needs (ie, physical, dietary, etc). Please contact Linda Sangenito prior to the live event at 732-992-1520.

For more information please visit www.CutaneousMalignancies.com
AGENDA

WEDNESDAY, OCTOBER 29
3:00 pm - 7:00 pm  Registration
5:30 pm - 7:30 pm  Welcome Reception/Exhibits

THURSDAY, OCTOBER 30
6:45 am - 9:15 am  Breakfast Product Theaters
9:15 am - 9:30 am  Break
9:30 am - 9:45 am  Welcome to the Third Annual World Cutaneous Malignancies Congress - Setting the Stage for the Meeting – Sanjiv S. Agarwala, MD
9:45 am - 11:45 am  General Session I
The Molecular Biology of Cutaneous Malignancies - Implications for Personalized Therapy
• Understanding the molecular biology of malignant melanoma: a clinical perspective – Antoni Ribas, MD
• The molecular basis of basal cell carcinoma (BCC) – James MacDonald
• Cutaneous T-cell lymphoma (CTCL): molecular aspects of disease development and response to targeted agents – Anjali Mishra, PhD
• Immunologic characterization of tumor cells in CTCL: application to clinical practice – Rachel Clark, MD, PhD
• Virus-positive and virus-negative Merkel cell carcinoma (MCC): implications for the clinician – Isaac Brownell, MD, PhD
Question & Answer Panel Discussion
11:45 am - 12:00 pm  Break
12:00 pm - 1:00 pm  Meet the Experts/Lunch in the Exhibit Hall
1:00 pm - 2:15 pm  General Session II
Current Treatment Algorithms in Cutaneous Malignancies
• Current approaches to therapy in malignant melanoma: the US perspective – Antoni Ribas, MD
• Current approaches to therapy in malignant melanoma: the EU perspective – Axel Hauschild, MD
• Current treatment options for advanced BCC – Karl Lewis, MD
• Current treatment options in CTCL – Pierluigi Porcu, MD
• Update on NCCN guidelines for the management of MCC – Christopher K. Bichakjian, MD
2:15 pm - 2:30 pm  Break
2:30 pm - 2:50 pm  Keynote Debate
International Focus on Melanoma: Case Presentation Followed by US vs EU vs Latin America Debate on Therapy – Sanjiv S. Agarwala, MD; Héctor Martínez Said, MD; Axel Hauschild, MD
2:50 pm - 4:35 pm  General Session III
Emerging Therapies, Combos, and Targeted Agents
• Changing arena of adjuvant therapy in malignant melanoma – Reinhard Dummer, MD, PhD

 Friday, October 31
7:00 am - 8:00 am  Breakfast
8:00 am - 8:15 am  Break
8:15 am - 8:30 am  Review of Thursday’s Presentations and Preview of Today’s Sessions – Sanjiv S. Agarwala, MD
8:30 am - 9:30 am  General Session IV
Prevention and Early Detection
• Early detection of primary tumors in melanoma – Susan M. Swetter, MD
• A new serologic assay for early detection of recurrent MCC – Paul Nghiem, MD, PhD
• An update on the SCREEN trial: skin cancer screening in Germany – Axel Hauschild, MD
Question & Answer Session
9:30 am - 9:45 am  Break
9:45 am - 11:10 am  Keynote Panel Discussion
Is There a Role for “Conventional Therapies” for Cutaneous Malignancies in the Era of Targeted Agents? – Sanjiv S. Agarwala, MD; Axel Hauschild, MD; Paul Nghiem, MD, PhD; Pierluigi Porcu, MD; Aleksandar Sekulic, MD, PhD
11:10 am - 11:25 am  Keynote Panel Discussion
11:25 am - 12:00 pm  Closing Remarks – Sanjiv S. Agarwala, MD
*Agenda subject to change.

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