You are cordially invited to attend an ERBITUX® (cetuximab) presentation

EGFR-Inhibitor-Related Dermatologic Toxicity Management: Considerations in Clinical Practice

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Program Information:
1254466
Thursday, September 10, 2015 at 6:00 PM
Frog and the Peach
29 Dennis Street
New Brunswick, NJ
(732) 846-3216

Meeting ID:
1254466

Program Faculty:
Kathleen Lynch, RN
Director of Nursing; Hematology Oncology
Association of Northern NJ
RCCA - Morristown Division,
Morristown, New Jersey

You have been cordially invited by:
John Finnegan, Earl Sirak &
Marva Fearon-Pierce

To RSVP:

To make a reservation, please call

1-888-451-RSVP (7787).

Please refer to Meeting ID when making your reservation.

In accordance with the PhRMA Code on Interactions with Healthcare Professionals, attendance at this educational program is limited to healthcare professionals. As such, attendance by guests or spouses is not permitted.

Federal and some state employees are restricted or prohibited from accepting food and beverages from pharmaceutical companies. Pharmaceutical companies are also required to report expenditures for food and beverages consumed by US licensed physicians and certain US healthcare professionals. By accepting any food or beverages offered at this program or engagement, I acknowledge that I am not prohibited from accepting these items and that Bristol-Myers Squibb will report the expense associated with these items as required by applicable federal and state law.

This invitation is non-transferable.

INDICATIONS

Head and Neck Cancer

ERBITUX® (cetuximab), in combination with radiation therapy, is indicated for the initial treatment of locally or regionally advanced squamous cell carcinoma of the head and neck (SCCHN).

ERBITUX is indicated in combination with platinum-based therapy with 5-FU for the first-line treatment of patients with recurrent locoregional disease or metastatic squamous cell carcinoma of the head and neck.

ERBITUX, as a single agent, is indicated for the treatment of patients with recurrent or metastatic squamous cell carcinoma of the head and neck for whom prior platinum-based therapy has failed.

Colorectal Cancer

ERBITUX is indicated for the treatment of *KRAS* wild-type, epidermal growth factor receptor (EGFR)-expressing, metastatic colorectal cancer (mCRC) as determined by FDA-approved tests for this use:

- in combination with FOLFIRI (irinotecan, 5-fluorouracil, leucovorin) for first-line treatment
- in combination with irinotecan in patients who are refractory to irinotecan-based chemotherapy
- as a single agent in patients who have failed oxaliplatin- and irinotecan-based chemotherapy or who are intolerant to irinotecan

Limitation of Use: ERBITUX is not indicated for treatment of *RAS*-mutant colorectal cancer or when the results of the *RAS* mutation tests are unknown.

Boxed WARNINGS

Infusion Reactions: **Serious infusion reactions occurred with the administration of ERBITUX in approximately 3% of patients in clinical trials, with fatal outcome reported in less than 1 in 1000. Immediately interrupt and permanently discontinue ERBITUX infusion for serious infusion reactions**

Cardiopulmonary Arrest: **Cardiopulmonary arrest and/or sudden death occurred in 2% of patients with squamous cell carcinoma of the head and neck treated in a clinical trial with ERBITUX and radiation therapy and in 3% of patients with squamous cell carcinoma of the head and neck treated in a clinical trial with European Union (EU)-approved cetuximab in combination with platinum-based therapy with 5-fluorouracil (5-FU). Closely monitor serum electrolytes, including serum magnesium, potassium, and calcium, during and after ERBITUX administration**

ERBITUX®
CETUXIMAB
INJECTION FOR INTRAVENOUS INFUSION
100 MG/50 ML & 200 MG/100 ML VIALS

Please see Important Safety Information, including **Boxed WARNINGS** on pages 2 and 3 and Full Prescribing Information included in the envelope.

Please understand that you can request your name and other information be removed from future Bristol-Myers Squibb contacts at any time by calling 1-877-920-0485. You can also mail requests to: PO Box 2899, Palatine, IL 60078-2899.

ERBITUX® (cetuximab) IMPORTANT SAFETY INFORMATION INCLUDING BOXED WARNINGS

Infusion Reactions

- **Grade 3/4 infusion reactions occurred in approximately 3% of patients receiving ERBITUX® (cetuximab) in clinical trials, with fatal outcome reported in less than 1 in 1000**
  - **Serious infusion reactions, requiring medical intervention and immediate, permanent discontinuation of ERBITUX, included rapid onset of airway obstruction (bronchospasm, stridor, hoarseness), hypotension, shock, loss of consciousness, myocardial infarction, and/or cardiac arrest**
  - **Immediately interrupt and permanently discontinue ERBITUX infusion for serious infusion reactions**
- **Approximately 90% of the severe infusion reactions were associated with the first infusion of ERBITUX despite premedication with antihistamines**
  - **Caution must be exercised with every ERBITUX infusion, as there were patients who experienced their first severe infusion reaction during later infusions**
  - **Monitor patients for 1 hour following ERBITUX infusions in a setting with resuscitation equipment and other agents necessary to treat anaphylaxis (eg, epinephrine, corticosteroids, intravenous antihistamines, bronchodilators, and oxygen). Longer observation periods may be required in patients who require treatment for infusion reactions**

Cardiopulmonary Arrest

- **Cardiopulmonary arrest and/or sudden death occurred in 4 (2%) of 208 patients with squamous cell carcinoma of the head and neck treated with radiation therapy and ERBITUX, as compared to none of 212 patients treated with radiation therapy alone. In 3 patients with prior history of coronary artery disease, death occurred 27, 32, and 43 days after the last dose of ERBITUX. One patient with no prior history of coronary artery disease died one day after the last dose of ERBITUX. Fatal cardiac disorders and/or sudden death occurred in 7 (3%) of the 219 patients with squamous cell carcinoma of the head and neck treated with platinum-based therapy with 5-fluorouracil (5-FU) and European Union (EU)-approved cetuximab as compared to 4 (2%) of the 215 patients treated with chemotherapy alone. Five of these 7 patients in the chemotherapy plus cetuximab arm received concomitant cisplatin and 2 patients received concomitant carboplatin. All 4 patients in the chemotherapy-alone arm received cisplatin**
  - **Carefully consider the use of ERBITUX in combination with radiation therapy or platinum-based therapy with 5-FU in head and neck cancer patients with a history of coronary artery disease, congestive heart failure or arrhythmias in light of these risks**
  - **Closely monitor serum electrolytes, including serum magnesium, potassium, and calcium during and after ERBITUX therapy**

Pulmonary Toxicity

- Interstitial lung disease (ILD), which was fatal in one case, occurred in 4 of 1570 (<0.5%) patients receiving ERBITUX in Studies 1, 3, and 6, as well as other studies, in colorectal cancer and head and neck cancer. Interrupt ERBITUX for acute onset or worsening of pulmonary symptoms. Permanently discontinue ERBITUX for confirmed ILD

Dermatologic Toxicities

- In clinical studies of ERBITUX, dermatologic toxicities, including acneiform rash, skin drying and fissuring, paronychial inflammation, infectious sequelae (eg, *S. aureus* sepsis, abscess formation, cellulitis, blepharitis, conjunctivitis, keratitis/ulcerative keratitis with decreased visual acuity, cheilitis), and hypertrichosis, occurred in patients receiving ERBITUX therapy.
  - Acneiform rash occurred in 76-88% of 1373 patients receiving ERBITUX in Studies 1, 3, 5, and 6. Severe acneiform rash occurred in 1-17% of patients. Acneiform rash usually developed within the first 2 weeks of therapy and resolved in a majority of the patients after cessation of treatment, although in nearly half, the event continued beyond 28 days
  - Life-threatening and fatal bullous mucocutaneous disease with blisters, erosions, and skin sloughing has also been observed in patients treated with ERBITUX. It could not be determined whether these mucocutaneous adverse reactions were directly related to EGFR inhibition or to idiosyncratic immune-related effects (eg, Stevens-Johnson syndrome or toxic epidermal necrolysis)
  - Monitor patients receiving ERBITUX for dermatologic toxicities and infectious sequelae
  - Sun exposure may exacerbate these effects

ERBITUX Plus Radiation Therapy and Cisplatin

- In a controlled study, 940 patients with locally advanced SCCHN were randomized 1:1 to receive either ERBITUX in combination with radiation therapy and cisplatin or radiation therapy and cisplatin alone. The addition of ERBITUX resulted in an increase in the incidence of Grade 3-4 mucositis, radiation recall syndrome, acneiform rash, cardiac events, and electrolyte disturbances compared to radiation and cisplatin alone
- Adverse reactions with fatal outcome were reported in 20 patients (4.4%) in the ERBITUX combination arm and 14 patients (3.0%) in the control arm
- Nine patients in the ERBITUX arm (2.0%) experienced myocardial ischemia compared to 4 patients (0.9%) in the control arm
- The addition of ERBITUX to radiation and cisplatin did not improve progression-free survival (the primary endpoint)

Electrolyte Depletion

- Hypomagnesemia occurred in 55% of 365 patients receiving ERBITUX in Study 5 and two other clinical trials in colorectal cancer and head and neck cancer, respectively, and was severe (NCI CTC grades 3 & 4) in 6-17%. In Study 2 the addition of EU-approved cetuximab to cisplatin and 5-FU resulted in an increased incidence of hypomagnesemia (14% vs 6%) and of grade 3-4 hypomagnesemia (7% vs 2%) compared to cisplatin and 5-FU alone. In contrast, the incidences of hypomagnesemia were similar for those who received cetuximab, carboplatin, and 5-FU compared to carboplatin and 5-FU (4% vs 4%). No patient experienced grade 3-4 hypomagnesemia in either arm in the carboplatin subgroup. The onset of hypomagnesemia and accompanying electrolyte abnormalities occurred days to months after initiation of ERBITUX therapy
  - Monitor patients periodically for hypomagnesemia, hypocalcemia, and hypokalemia, during, and for at least 8 weeks following the completion of, ERBITUX therapy
  - Replete electrolytes as necessary

Increased Tumor Progression, Increased Mortality, or Lack of Benefit in Patients with *RAS*-Mutant mCRC

- ERBITUX is not indicated for the treatment of patients with colorectal cancer that harbor somatic mutations in exon 2 (codons 12 and 13), exon 3 (codons 59 and 61), and exon 4 (codons 117 and 146) of either *KRAS* or *NRAS*

continued on next page

Please see accompanying Full Prescribing Information included in the envelope.