Trainee Research-in-Progress Submission Example

Title: Lack of Adequate Pneumococcal Vaccination Response in Chronic Lymphocytic Leukemia Patients Receiving Ibrutinib

Category of Presentation: Clinical Research

Topic of Presentation: Supportive Care

Abstract Text:

Background
Chronic lymphocytic leukemia (CLL) is characterized by a dysfunction of innate and adaptive mediated immunity and subsequently infections are commonly incurred by patients. The CDC recommends CLL patients to receive the 13-valent pneumococcal conjugated vaccination (PCV13) to reduce the risk of infection. Ibrutinib, an irreversible inhibitor of Bruton tyrosine kinase (BTK), has been associated with the development of pneumonia in 4-18% of patients. BTK is essential for B cell function and development as well as Toll-like receptors which are involved in innate and adaptive immunity.

Objective
This study evaluated the effectiveness of PCV13 vaccination between CLL patients treated with ibrutinib and active surveillance (control) by assessing anti-pneumococcal antibody generation following vaccination. Secondarily this study investigated BTK and SAMSN1 (hematopoietic adapter containing SH3 and SAM domain 1) expression following vaccination.

Methods:
This IRB approved, prospective, single-center, non-blinded study evaluated immunization response of PCV13 in 2 study cohorts (ibrutinib or control). All eligible patients provided written consent. At Day 0 (vaccination) both study cohorts received a single dose (0.5mL) of PCV13. Peripheral blood samples (8mL) were collected on day 0 and 30. Serum pneumococcal antibody generation was assessed with microsphere photometry for antibody specific serotypes (1, 3, 4, 5, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23) and analyzed by Lumniex 200 instrument. Adequate immunization response was defined by a ≥ 2-fold increase of ≥ 3 of pneumococcal serotypes. Mononuclear cells were isolated using Ficoll-Hisotopaque 1077 density gradient and CD19+ B-lymphocyte isolation was performed using Dynabeads® CD19 pan B. Subsequently, Western blot analysis was performed to identify BTK and SAMSN1 expression at day 0 and 30.
Results:
Eight patients (n=4 ibrutinib, n=4 control) were enrolled with a median patient age of 69 yo (75% > 65yo). All CLL control patients (4/4) generated an adequate immunological response, whereas (0/4) of ibrutinib patients generated an adequate immune response to PCV13 (p=0.029; post-hoc Fisher exact). Five PCV serotypes: 1 (p=0.03), 3 (p=0.03), 5 (p=0.01), 6B (p=0.009), and 18C (p=0.03) were significantly increased at Day 30 in control patients. Overall there was a significant increase in the median change of specific pneumococcal antibody titers in the control group (p<0.0001; CI 90.9-124.7). Elevated SAMSNI expression was identified in pre-vaccination ibrutinib patients (p<0.0115) and mechanistically could explain impaired immunization response.

Conclusions:
PCV13 vaccination in CLL patients receiving ibrutinib does not induce an adequate vaccination response. Given these results, additional evaluation to improve immunogenicity of pneumococcal vaccination in ibrutinib patients is warranted.

See ePoster here
Trainee Research-in-Progress Submission Example

Title: Characterization of Marijuana Use in Cancer Patients Receiving Chemotherapy

Category of Presentation: Practice Management

Topic of Presentation: Supportive Care

Abstract Text:

Background
Marijuana has been suggested as a supportive care agent to manage side effects associated with chemotherapy. As legalization of medical and recreational marijuana increases throughout the United States, it is possible that use amongst cancer patients will increase. Previously, little was known regarding the prevalence and demographics of those who choose to use marijuana for side effect management while receiving chemotherapy.

Objective
Primary outcome: The primary outcome of this research will thoroughly characterize the demographics and health status of patients who use and do not use medical marijuana as adjunctive therapy in treating chemotherapy induced side effects. Secondary Outcome: The secondary outcome will further characterize those who choose to use medical marijuana to treat their chemotherapy induced side effects.

Methods:
An anonymous, self-administered, and voluntary survey was provided to patients in the infusion center at the University of Colorado Cancer Center. The survey included questions on marijuana use history, reasons for using or abstaining, clinical characteristics and demographics.

Results:
Fifty-three (28.6%) of the 185 patients surveyed reported use of marijuana within the past 6 months. Forty-three (23.3%) patients reported former use and 89 (48.1%) reported having never used marijuana. Forty-one of the current users (77.4%) reported using marijuana to manage the side effects of chemotherapy with the most common reason to use marijuana being to nausea and vomiting (n=29, 54.7%). Current marijuana use was associated with younger age (p=0.002), use of complementary and alternative medicine (p<0.001) and higher side effect frequency scores (p<0.001). Of all respondents, 41 (22.16%) reported that their oncology provider asks about marijuana use.
Conclusions:
The results of this survey demonstrate that cancer patients who use marijuana are not representative of marijuana users in the general population with cancer patients having higher use. Additionally, there are very few demographic and clinical differences between oncology patient marijuana users and non-users, with age being the only difference. Education level, employment, income, and gender were similar between groups. Of those who choose to use marijuana, it is most commonly used to manage side effects associated with chemotherapy and users have higher side effect frequency scores compared to non-users. With legalization increasing throughout the country and high prevalence rates in cancer patients, providers should increase discussions surrounding safe and appropriate use of marijuana.

See ePoster Here
Peripheral blood samples (~15 mL) at Day 0 (prior to PCV13 administration) and Day +30

Mutated

Ibrutinib, a Bruton’s tyrosine kinase inhibitor (BTK), inhibits Btk and \( \beta \)-actin expression between the control (Ctrl) and ibrutinib (Ibr) cohorts.

**METHODS**

- Peripheral blood samples (~15 mL) at Day 0 (prior to PCV13 administration) and Day +30
- Pneumococcal Antibody Panel Test (Mayo Medical Laboratories\(^a\)) - Microsphere Photometry to identify the presence and concentration of anti-pneumococcal IgG titers against serotypes 1, 3, 4, 5, 9, 12F, 14, 19F, 23F, 6B, 7F, 18C
- Separation and peripheral blood mononuclear cell (PBMC, lymphocytes) isolation via Ficol following cryopreservation.
- B-lymphocyte isolation - Dynabeads CD19 Pan B\(^b\)
- Western Blot analysis
  - Anti-SAMSN1 (HACS1) rabbit polyclonal antibody (Abcam\(^c\) ab139735)
  - BTK rabbit monoclonal antibody (Cell Signaling Technology\(^c\) 8288)

**RESULTS**

<table>
<thead>
<tr>
<th>Table 1: Patient Demographics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subject</td>
</tr>
<tr>
<td>---</td>
</tr>
<tr>
<td>1</td>
</tr>
<tr>
<td>2</td>
</tr>
<tr>
<td>3</td>
</tr>
<tr>
<td>4</td>
</tr>
</tbody>
</table>

**ENDPOINTS**

- **Data analysis:**
  - Satisfactory immune responses for anti-pneumococcal antigen generation defined as ≥2-fold titer increase post-vaccination in ≥ 3 serotypes
  - Pre and post-vaccination expression of HACS1 and BTK will be evaluated with densitometry using NIH Image J software

- **Statistical analysis:**
  - Pneumococcal serotypes – Chi Square
  - HACS1 and BTK – Student’s two-sided t-test

**Table 2: Anti-Pneumococcal IgG Seroprotective Titer**

<table>
<thead>
<tr>
<th>Serotype</th>
<th>Ibrutinib Cohort (n=4)</th>
<th>Control Cohort (n=4)</th>
<th>Day 0</th>
<th>Day 30</th>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.1</td>
<td>1.3</td>
<td>0.2</td>
<td>22.6</td>
<td>112.2</td>
</tr>
<tr>
<td>3</td>
<td>0.7</td>
<td>0.6</td>
<td>-0.1</td>
<td>2.2</td>
<td>18.9</td>
</tr>
<tr>
<td>4</td>
<td>0.4</td>
<td>0.3</td>
<td>-0.1</td>
<td>5.9</td>
<td>12.1</td>
</tr>
<tr>
<td>5</td>
<td>1.7</td>
<td>1.6</td>
<td>-0.1</td>
<td>6.1</td>
<td>112.8</td>
</tr>
<tr>
<td>14</td>
<td>2.4</td>
<td>1.6</td>
<td>-0.8</td>
<td>6.1</td>
<td>112.8</td>
</tr>
<tr>
<td>19F</td>
<td>3.2</td>
<td>5.1</td>
<td>1.9</td>
<td>7.1</td>
<td>12.4</td>
</tr>
<tr>
<td>23</td>
<td>4.3</td>
<td>3.6</td>
<td>-0.7</td>
<td>9.8</td>
<td>33.3</td>
</tr>
<tr>
<td>6B</td>
<td>3.1</td>
<td>3.3</td>
<td>-0.2</td>
<td>4.4</td>
<td>30.8</td>
</tr>
<tr>
<td>7F</td>
<td>1.6</td>
<td>2.1</td>
<td>-0.4</td>
<td>7.0</td>
<td>13.1</td>
</tr>
<tr>
<td>18C</td>
<td>0.9</td>
<td>0.6</td>
<td>-0.3</td>
<td>2.2</td>
<td>21.4</td>
</tr>
<tr>
<td>19A</td>
<td>2.5</td>
<td>2.3</td>
<td>-0.2</td>
<td>9.2</td>
<td>31.5</td>
</tr>
<tr>
<td>39V</td>
<td>3.4</td>
<td>3.0</td>
<td>-0.4</td>
<td>6.2</td>
<td>4.7</td>
</tr>
</tbody>
</table>

**DISCUSSION**

- All control patients (4/4) generated an adequate immune response versus (0/4) ibrutinib patients (p=0.029)
- Significant increase in the median change of specific pneumococcal antibody titers in the control vs ibrutinib group (p<0.0001; CI 90.3-124.7)
- Ibrutinib therapy results in a decrease or no change in antibody generation versus baseline
- SAMSN1 pre-vaccination expression was elevated for pts on ibrutinib

**Conclusions**

- In this pilot study, CLL patients receiving ibrutinib were unable to mount an adequate immune response to PCV13
- Highlights need to address vaccinations before initiating novel oral oncologic therapies

**REFERENCES**

MARIJUANA USE IN CANCER PATIENTS RECEIVING CHEMOTHERAPY

Jade Bryant PharmD Candidate & Cindy L. O’Byant PharmD, BCOP, FCCP, FHOPA
University of Colorado Skaggs School of Pharmacy and Pharmaceutical Sciences Aurora, CO, USA

Introduction

• Marijuana is used by cancer patients to manage side effects associated with chemotherapy.
• As legalisation of medical and recreational marijuana increases throughout the US, it is possible that use among cancer patients will increase.
• Colorado is a unique environment to study marijuana use due to the recreational and legal status of the state.
• Little is known about the prevalence, demographics, reasons for use and sources of information regarding use of marijuana in cancer patients.

Objectives

Primary Objective: The primary objective of this research is to characterize the demographics and health status of patients who use and do not use medical marijuana as an adjunctive therapy in managing chemotherapy induced side effects.

Secondary Objective: The secondary outcome of this research is to further characterize those who choose to use medical marijuana.

Methods

• Voluntary, anonymous survey of patients in the outpatient infusion center at the University of Colorado Cancer Center for a period of one month.
• Surveys were collected from August 2015 – December 2016.
• The survey is a 34 question instrument, which can be completed in 5-10 minutes.
• The survey was created based on previous literature assessing complementary and alternative medicine (CAM) use in cancer patients.
• This study was approved by the Institutional Review Board at the University of Colorado Hospital and the Protocol Review and Monitoring System at the University of Colorado Cancer Center.
• Data was collected and stored in REDCap.

Analysis

• Descriptive Statistics
• Data was analyzed using SPSS software.

• Chi-square or Fisher’s exact test were used to analyze categorical or difference of means respectively.

• A symptom frequency score was determined from the following:

• Sum of how often patients reported experiencing nausea/emesis, diarrhea/constipation, hair loss, fatigue, pain and anxiety/weight loss on a scale from 1-5.

Results

Comparison of Users and Non-Users

Table 1: Characteristics of Users and Non-Users

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Users</th>
<th>Non-Users</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>41.04±9.16</td>
<td>41.52±9.74</td>
<td>0.886</td>
</tr>
<tr>
<td>Gender</td>
<td>22 (76.7%)</td>
<td>33 (77.3%)</td>
<td>0.706</td>
</tr>
<tr>
<td>Ethnicity</td>
<td>27 (93.1%)</td>
<td>38 (87.2%)</td>
<td>0.271</td>
</tr>
<tr>
<td>Education Level</td>
<td>25 (86.2%)</td>
<td>38 (87.2%)</td>
<td>0.904</td>
</tr>
<tr>
<td>Marijuana Use</td>
<td>Yes</td>
<td>No</td>
<td>0.001</td>
</tr>
<tr>
<td>Marijuana Use Duration</td>
<td>2 (33.3%)</td>
<td>6 (33.3%)</td>
<td>1.000</td>
</tr>
<tr>
<td>Marijuana Use Frequency</td>
<td>Once a Week</td>
<td>Twice a Week</td>
<td>0.001</td>
</tr>
<tr>
<td>Marijuana Use Form</td>
<td>Smoke</td>
<td>Tincture</td>
<td>0.001</td>
</tr>
<tr>
<td>Marijuana Use Source</td>
<td>Dispensary</td>
<td>Medication</td>
<td>0.001</td>
</tr>
<tr>
<td>Marijuana Use Comp. Use</td>
<td>Yes</td>
<td>No</td>
<td>0.001</td>
</tr>
<tr>
<td>Marijuana Use Health Use</td>
<td>Yes</td>
<td>No</td>
<td>0.001</td>
</tr>
<tr>
<td>Marijuana Use Cost</td>
<td>No</td>
<td>Yes</td>
<td>0.001</td>
</tr>
<tr>
<td>Marijuana Use Sensations</td>
<td>No</td>
<td>Yes</td>
<td>0.001</td>
</tr>
<tr>
<td>Marijuana Use Age</td>
<td>20-49</td>
<td>10-19</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Surveying health care providers about their willingness to discuss marijuana use with patients and barriers to communications.

Younger age, more frequent side effects, and CAM use are associated with those who choose to use marijuana during chemotherapy.

Data was analyzed using SPSS software.

Results, Continued

Table 2: Characterization of marijuana use

<table>
<thead>
<tr>
<th>Characterization of Marijuana Use</th>
<th>Users</th>
<th>Non-Users</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marijuana Use</td>
<td>Yes</td>
<td>No</td>
<td>0.001</td>
</tr>
<tr>
<td>Marijuana Use Duration</td>
<td>2 (33.3%)</td>
<td>6 (33.3%)</td>
<td>1.000</td>
</tr>
<tr>
<td>Marijuana Use Frequency</td>
<td>Once a Week</td>
<td>Twice a Week</td>
<td>0.001</td>
</tr>
<tr>
<td>Marijuana Use Form</td>
<td>Smoke</td>
<td>Tincture</td>
<td>0.001</td>
</tr>
<tr>
<td>Marijuana Use Source</td>
<td>Dispensary</td>
<td>Medication</td>
<td>0.001</td>
</tr>
<tr>
<td>Marijuana Use Comp. Use</td>
<td>Yes</td>
<td>No</td>
<td>0.001</td>
</tr>
<tr>
<td>Marijuana Use Health Use</td>
<td>Yes</td>
<td>No</td>
<td>0.001</td>
</tr>
<tr>
<td>Marijuana Use Cost</td>
<td>No</td>
<td>Yes</td>
<td>0.001</td>
</tr>
<tr>
<td>Marijuana Use Sensations</td>
<td>No</td>
<td>Yes</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Survey cancer patient populations at hospitals throughout Colorado with different demographics to investigate various prevalence levels throughout the state.

Discussion

• Fifty-three (28.6%) of the 185 patients surveyed reported use of marijuana within the past 6 months, where only 12.3% of Coloradans 21 years or older are current users.
• Cancer patients who are marijuana users are:
  • more likely to use CAM products (<0.001) and experience chemotherapy side effects more frequently (p<0.001)
  • more likely to be 40-60 years old and are less likely to use if they are 70 years or older.
  • Providers do not frequently ask about marijuana use.
  • The most common source of information is from the dispensary or family and friends.
  • Most patients use marijuana to manage side effects associated with chemotherapy and not for treating the cancer itself.
  • Poor coordination is reported as the most common side effect with an equal amount of respondents reporting no side effects.

Conclusion

• Cancer patients who use marijuana are not representative of marijuana users in the general population, they have a higher rate of use and less predictors of use.
• Younger age, more frequent side effects, and CAM use are associated with those who choose to use marijuana during chemotherapy treatment.
• Use of marijuana was reported to be tolerable and the side effects did not seem to add to chemotherapy or supportive care medication side effects, however more research regarding the efficacy and safety of marijuana use is needed.
• Pharmacists and other health care providers should look for opportunities to provide evidence based information regarding marijuana use during chemotherapy.

The next steps for this work include:

• Surveying health care providers about their willingness to discuss marijuana use with patients and barriers to communications.

• Analysis of how to best dispense information to patients who use marijuana.
• Survey cancer patient populations at hospitals throughout Colorado with different demographics to investigate various prevalence levels throughout the state.

References

1. Skaggs School of Pharmacy and Pharmaceutical Sciences.