

IMPLEMENTING EVIDENCE BASED GUIDELINES FOR IMMUNE CHECKPOINT
INHIBITORS IN A COMMUNITY ONCOLOGY CLINIC

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PRACTICE

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Abstract

Aim: Improve patient safety for patient's receiving immune checkpoint inhibitor therapy by implementing evidenced based guidelines

Background: Immuno-oncology (I/O) is a growing field in oncology. Immune checkpoint inhibitors (ICIs) are the most common type of I/O. Side effects from ICI differ from chemotherapy. Incidence of immune mediated adverse events (irAEs) have been documented as high as 90%, with severe toxicities being reported as high as 48% in clinical trials. National published guidelines are available for assessment and treatment of irAEs, however, are not routinely implemented in community oncology clinics.

Methods: Using the RE-AIM framework, this project's aim was to improve the safety for patients receiving ICI therapy at a community oncology clinic by: establishing baseline patient assessment prior to the start of ICI therapy; providing ICI specific patient education; issuing ICI patient wallet card and updating ICI oncology modules to meet current guidelines.

Results: During project implementation 9/15-12/15/20: 92% of patients starting ICI therapy had a baseline assessment; received ICI specific education and were issued a wallet card. Ninety-four percent of ICI oncology modules were updated meeting current guidelines. In addition, staff found to the project to be sustainable, useful, of high quality, easy to follow and met clinic needs.

Implications: Immunotherapy is a growing field in oncology and many tertiary/academic cancer centers have dedicated I/O clinics. Community oncology (where the majority of patients are treated) are unable to support I/O clinics such as these. Implementation of evidenced based guidelines in a community setting ultimately improves the quality of care and safety of patients receiving ICI therapy.

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Introduction

Immuno-oncology (IO) has changed the landscape of cancer care, improving outcomes for many patients with different tumor types. Along with these positive responses have come a new set of adverse events. The incidence of immune-related adverse events (irAEs) is lower when compared to conventional chemotherapy; however, irAEs can last longer and be more detrimental (NCCN, 2019). Oncology clinicians, including nurses, have to change the way they think about educating and managing patients who receive IOs. It has been difficult for the oncology specialty to manage irAEs effectively as they differ from classic chemotherapy side effects. Delayed recognition of irAEs can be severe or even fatal (Cole, Zibelman, Bertino, Yucebay, & Reynolds, 2019). Many academic and tertiary cancer centers have developed specific IO clinics to treat patients on immunotherapy and there have been specific guidelines developed to assist with management of patients. (Hoffner & Rubin, 2019).

The National Comprehensive Cancer Network (NCCN) and multiple other oncology professional organizations such as the American Society for Clinical Oncology (ASCO) and the Society for Immunotherapy of Cancer (SITC) have developed guidelines for monitoring and treating irAEs. However, as these guidelines have become the standard of care very quickly, community oncology clinics and practices have struggled with implementing them due to limited resources. It is the intention of this DNP project to work with Hawaii Pacific Health (HPH) in implementing current guidelines, as there has not been any formal implementation with these guidelines to date.

Needs Assessment

Based upon experience and discussion with oncology providers and administrators at HPH, the following gaps were identified in the needs assessment:

- The need to standardize methods of patient education
 - Providers to give education to patients/family
 - Materials are given to patients
 - Workflow for reporting symptoms
- The need to identify patients who have received immunotherapy
 - Provide patients with wallet cards
- The need for pre-therapy assessment is done as per NCCN guidelines (Version 1.2020)
- The need to for pertinent lab work is done at baseline and prior to each cycle as per NCCN guidelines (Version 1.2020)
 - If abnormalities are detected, assure additional testing is ordered for ongoing monitoring and further work-up/management is being implemented per current NCCN guidelines
- The need to for recommended baseline and ongoing assessment testing is implemented either by embedding in Beacon orders (Epic Systems' medical oncology module) and/or developing a clear workflow for assessment
 - i.e.-Oxygen saturation (resting and ambulation) for potential pneumonitis for all patients with primary lung cancer and/or lung metastases as the incidence of this irAE is higher in this group of patients (NCCN, 2020 & Nishino, Sholl, Hatabu, Ramaiya, & Hodi, 2015)

- The need to identify key clinicians such as APRNs and nurse navigators in the education and management of emergent irAEs

Background/Significance

Currently, there are multiple immune checkpoint inhibitors (ICIs) available for cancer treatment. Approved agents include the programmed death 1(PD-1) inhibitors: Pembrolizumab, Nivolumab, Cemiplimab; the program death ligand-1 (PD-L1) inhibitors: Atezolizumab, Avelumab, Durvalumab; and the human cytotoxic T-lymphocyte antigen-4 blocking antibody: Ipilumab (Trin, et al., 2019). The incidence of irAEs for PD-1 & PD-L1 inhibitors are estimated at about thirty percent based on the National Cancer Institute's Common Terminology Criteria for Grading Adverse Events (CTCAE), with grade 3 and 4 toxicities reported at six percent; while the incidence for CTLA-4 have been estimated as high as ninety percent with grade 3 and 4 (see Appendix A) being reported as high as 48% (Valsco, et al., 2017; Eggermont, et al., 2015 & Wang, et al. 2017). The U.S Food and Drug Administration (FDA) approvals of indications for ICIs have occurred at an unprecedented rate in single agent use and in combination regimens (Brahmer, et al., 2018).

As the indications for ICIs continue to grow along the landscape of cancer treatments, the incidence and prevalence of immune-mediated adverse events, (irAEs) are still fully elucidated. Despite the often-durable clinical benefits of ICIs, their use is associated with a spectrum of adverse events-related to the underlying mechanism of action of stimulating the immune system (Brahmer, et al., 2018). IrAEs can affect any organ at any time, however, the main organ systems that continue to emerge as most commonly affected are: dermatologic, gastrointestinal, endocrine and pulmonary (Velasco, et al., 2017).

Dermatologic irAEs most commonly include rash and pruritus with more rare events such as vitiligo, Stevens-Johnson syndrome, Sweet's syndrome, toxic epidermal necrolysis, bullous, pemphigoid and lichen sclerosis also have been reported (Dine, Gordon, Shames, Kasler, & Barton-Burke, 2017). Rash and pruritus usually occur early and are observed in about 30-40% percent of patients receiving ICIs (Davies & Duffield, 2017). Skin toxicities are typically low grade and often present with an erythemic papular rash on the trunk or extremities. Grade 1 dermatologic toxicities are treated with topical steroids and ICI therapy can be continued, however, grade 2 toxicities often require oral steroids and ICI therapy may be held. For grade 3 & 4 toxicities, ICI therapy is held and oral steroids are administered to control symptoms (NCCN, 2020).

The second most common organ system affected by irAEs is the gastrointestinal (GI) system, with immune-mediated colitis being reported in 23-41% of patients receiving ipilumab. It is not common with the PD-1 & PD-L1 inhibitors but still of concern. Clinical presentation includes watery bowel movements, flatulence and abdominal cramping. Autoimmune-mediated hepatitis is another GI irAEs that usually presents as asymptomatic elevations in liver function tests (LFT). Again, treatment can often be continued with low-grade GI grade toxicity. However, the clinician needs to be astute in treating with antidiarrheal medication for colitis and monitoring LFTs for hepatitis. If symptoms are progressive, treatment needs to be held and steroids need to be started or the irAEs could become life-threatening (Dine, et al., 2017 & NCCN, 2020).

Endocrinopathies are commonly seen with ICI treatment. The incidence among all ICIs is about 30%. Hypothyroidism is the most common; however, hyperthyroidism, thyroiditis, hypophysitis, adrenal insufficiency and diabetes mellitus are other possible irAEs. Lab changes

are usually seen before symptoms. Primary thyroid issues are treated with thyroid replacement or suppression, hypophysitis, and adrenal insufficiency are treated with replacement steroids. (Davies & Duffield, 2017 & NCCN, 2019).

Once thought to be rare when patients were treated on clinical trials, immune-mediated pneumonitis is now believed to affect about 10% in primary lung cancer patients being treated on standard of care ICI regimens. Reduced lung capacity due to pre-existing lung disease and prior chest radiation may increase one's risk for developing pneumonitis. Signs and symptoms of pneumonitis include cough, chest pain, fever, decreased O2 saturation and ground-glass infiltrates seen on imaging. Pneumonitis can be difficult to differentiate from clinical progression in advanced lung cancer patients. Treatment usually begins with holding ICI therapy and instituting steroids when patients have grade 2 symptoms (Dafni, et al., 2019, Davies & Duffield, 2017 & NCCN, 2019).

A wide array of other irAEs have been observed at low incidence in patients receiving ICI therapy across other organ systems, including neurological, ocular, musculoskeletal, hematologic, cardiac, pancreatic and renal. The incidence of these rare irAEs are approximately 1-2%, however, may be higher in patients receiving combination ICI therapy or ICIs in combination with chemotherapy or targeted therapies (Davies & Duffield, 2017).

Overall, the incidence of irAEs can be challenging to discern because there has been no standardized method to specify clinical criteria for grading irAEs. Clinical trials reporting the incidence of irAEs used the CTCAE that was developed for grading chemotherapy toxicities. Oncology clinicians including advanced practice registered nurses (APRNs) and other oncology nurses need to be cognizant of the importance of baseline physical assessment, lab monitoring,

and patient education, as well as the ongoing need for these skills as irAEs can develop while patients are on ICI therapy and long after they have completed ICI therapy.

Literature Synthesis

PubMed and CINAHL databases were used to search for the majority of the articles for this review. Additional articles based on references for articles were identified as well. Search terms used were “Oncology and Immune check-point-inhibitors”; “Oncology and Immune-mediated adverse events”, “Oncology and Immune Checkpoint inhibitors and nursing”, “Immune checkpoint inhibitors and APRN and “IrAE management”. Criteria for the articles included publication between the years 2014-2019; however, most articles reviewed were published in the past three years - as this is emerging information and science.

Approximately seventy-five abstracts were reviewed and critiqued for this synthesis. In the end, eighteen articles met all inclusion criteria and were included in this synthesis. In addition, four national guidelines for irAE management were reviewed: American Society for Clinical Oncology (ASCO), European Society for Medical Oncology (ESMO), National Comprehensive Cancer Network (NCCN), and Society for Immunotherapy of Cancer (SITC).

Mosby’s level of evidence was used to evaluate the strength of the included articles (Ackley, 2008). Please see Appendix B for the table of evidence. The literature is divided into different themes relevant to the project; they include irAE management, irAEs and nursing management, including the role of APRN and ICI patient education.

IrAE and management. Supported by the four major consensus guidelines of ASCO, ESMO, NCCN and SITC, the evidence was consistent in recommending corticosteroids as the mainstay of treatment for irAEs for dermatologic conditions. The four consensus guidelines

agree on how to treat grade 1 and grades 3 & 4 dermatologic toxicities. However, when making adjustments for grade 2 dermatitis, ESMO and SITC recommends continuing ICI therapy and continuing topical treatment. In contrast, ASCO and NCCN recommend clinicians consider withholding therapy and initiating high dose systemic steroids. All guidelines recommend a baseline dermatologic exam be performed prior to starting ICI therapy (Brahmer, et al., 2018, Haanen et al., 2017; NCCN, 2019 & Puzanov, et al., 2017).

Regarding gastrointestinal (GI) irAEs, all the guidelines support withholding ICI therapy and initiating high-dose corticosteroids for grade 2 toxicities. A GI consult is also recommended for patients experiencing grade 2 or higher GI toxicities. However, it is imperative to note that in the setting of steroid-refractory immune-mediated hepatitis, infliximab is not recommended as it can worsen hepatitis. This is an essential point as infliximab is recommended for use in almost every other steroid refractory irAE, including colitis. NCCN recommends documentation of baseline bowel habits and LFTs for all patients prior to starting ICI therapy and prompt work-up for blood in the stool and/or fever associated with loose stools (Brahmer, et al., 2018, Haanen et al., 2017; NCCN, 2019 & Puzanov, et al., 2017).

ICI-related endocrine dysfunction can affect the thyroid, pituitary, adrenal glands and the pancreas. It is important for the clinician to identify whether the endocrine dysfunction is primary or central to treat the patient appropriately. Referral to an endocrinologist is an important aspect of the management of endocrine irAEs due to their potential complexity. For hypothyroidism, both NCCN & SITC guidelines recommend thyroid supplementation and the monitoring of TSH and free T4 every 4-6 weeks for any grade event, whereas ESMO and ASCO recommend thyroid replacement in symptomatic patients. All four guidelines agree that ICIs should be held for grade 3 and 4 events until symptoms resolve. Of note, hypophysitis is not

recognized by SITC but addressed by the other three consensus guidelines. It is key for the clinician to recognize that this irAE is much common with the CTLA-4 inhibitor ipilimumab. Also essential, is that the main approach to hypophysitis management is to hold ICI therapy for any grade until resolution and administer supportive care and hormone replacement. Furthermore, recommendations for the administration of corticosteroids vary between the guidelines. It is recommended that baseline TSH, FT4, and serum cortisol are drawn and rechecked at least every four weeks while on ICI therapy and every 12 weeks after ICI therapy has completed as indicated. Also, NCCN recommends additional testing for abnormal findings and symptoms (Brahmer, et al., 2018, Haanen et al., 2017; NCCN, 2019 & Puzanov, et al., 2017).

Finally, pneumonitis is also recognized by NCCN, ASCO, ESMO and SITC as an irAE. All four-consensus guidelines agree that for pneumonitis of any grade that ICI therapy should be discontinued. It is recommended that grade 2 pneumonitis be treated with corticosteroids and empiric antibiotics as per ASCO & ESMO; however, NCCN & SITC do not recommend the routine use of empiric antibiotics in this setting. All four guidelines recommend permanently discontinuing ICI therapy for grades 3 or 4 pneumonitis. NCCN further discusses inpatient treatment for severe pneumonitis with a complete infectious workup and bronchoscopy and a consult with pulmonology and infectious disease. Again, infliximab is recommend for steroid refractory pneumonitis. Baseline oxygen saturation at rest and while ambulating is recommended before starting ICI therapy for all patients. In addition, NCCN recommends high-risk patients undergo pulmonary function tests prior to starting therapy. Additional workup is recommended for other abnormal findings and symptoms. (Brahmer, et al., 2018, Haanen et al., 2017; NCCN, 2019; Puzanov, et al., 2017 & Trinh, Le, Gowani, & La-Beck, 2019).

Each of the four guidelines further discuss management of rare irAEs such as: myocarditis, myositis and pancreatitis, however, it is beyond the scope of this literature synthesis to discuss these recommendations (Brahmer, et al., 2018; Haanen et al., 2017; NCCN, 2019; Puzanov, et al., 2017).

IrAEs and nursing management. Nursing management was addressed in several articles reviewed as well as the NCCN guidelines. Cole, et al. recognized the importance of nurse educators and nurse navigators in treating patients on ICIs. Whether through direct patient contact, staff education or facilitating system-based initiatives, Cole et al. highlighted that irAE management would be impossible without nursing integration at all levels (2019). Oncology Advanced Practice Providers (APPs) including APRNs were recognized as being integral in irAE management and helping to build a framework in one's institution to handle irAEs better. In addition, Oncology APPs are essential in monitoring and early management of irAEs preventing serious and/or life-threatening situations (Hoffner & Rubin, 2019; Hoffner, Vaughn, Reed, & Webb, 2019, 2019 Mistry, et al., 2017 & Wood, 2019). Both APRNs and nurses also play a critical role in baseline assessment prior to starting ICI therapy and before every infusion (Daniels, 2019; Davies & Duffield, 2017; Dine, et al., 2017; Gordon, et al., 2017; Lewis, 2016). Finally, several authors also review the key role of the nurse and APRN in the role as a patient educator (Davies, 2017; Davies & Duffield, 2017; Dine, et al., 2017, Gordon, et al., 2017; Hoffner & Rubin, 2019; Hoffner, et al., 2019; Lewis, 2016; Mistry, Forbes & Fowler, 2017; Wood, 2019 & Wood, Moldwater, & Lewis, 2019)

ICI patient education. Patient education has been identified as key in the early identification and management of irAEs. Educating patients that irAEs present differently than traditional chemotherapy side effects and at different times are key points to patient education

(Andrews, 2017; Cole, Zibelman, Bertino, Yucebay, & Reynolds, 2019, Davies, 2017; Davies & Duffield, 2017; Dine, et al., 2017, Gallioto, et al., 2019; Gordon, et al., 2017; Hoffner & Rubin, 2019; Hoffner, et al., 2019; Lewis, 2016; Mistry, et al., 2017; Seery, 2017; Wood, 2019 & Wood, et al., 2019). Several authors recommend that patients be provided with wallet cards for identification and correct management of these irAEs when patients present in urgent care clinics and emergency departments (Cole, et al., 2019, Daniels, 2019; Davies, 2017; Davies & Duffield, 2017; Gallioto, et al., 2019; NCCN, 2020 & Wood, et al., 2019).

Wood, et al., 2019, discusses five key points to include when educating patients: Background and mechanism of action (MOA) of ICIs, expected response to treatment, monitoring and management of side effects, when to expect side effects and when to contact the cancer team. She points out that, ICI patient education tools are in the early stages, but the importance of providing unique ICI education apart from conventional chemotherapy has become increasingly recognized. The importance of standardized patient education has already been documented in the oncology arena and has not only been shown to improve patient outcomes, but also reduce anxiety (Apor, et al, 2018; Garcia, 2014; Hoff & Tonne, 2017; & Valenti, 2014).

Problem

Problem: There has not been ICI guidelines implemented for patients receiving ICIs at HPH.

Population: For oncology patients receiving ICIs

Intervention:

- Implement baseline assessment and monitoring for irAEs as per NCCN guidelines

- Create evidence based educational materials for patients receiving immunotherapy

Comparison: Present practice within oncology clinics

Outcome/Timing: By the end of this DNP project (May 2021), HPH will have clear evidenced based immunotherapy guidelines in place with adequate patient education, baseline assessment and testing.

Purpose statement

It was the intention of this DNP project to work with HPH in implementing current guidelines NCCN guidelines, for pre-assessment and lab monitoring as well as standardize patient education based on the evidence to improve the management of oncology patients who receive ICIs, as there had not been any formal implementation in compliance with these guidelines to date.

Theoretical framework

To implement the practice changes of this DNP project into Straub oncology clinic, the author used the Reach, Effectiveness, Adoption, Implementation and Maintenance (RE-AIM) framework (RE-AIM, 2020). By utilizing the RE-AIM framework, the author was able to: 1) identify the population to be **reached**, 2) define the **efficacy** of the intervention, 3) describe the who will need to be engaged to make the **adoption** of project successful, 4) explain the **implementation** process and 5) discuss how the project will be **maintained** after the initial phase.

Project Goals and Objectives

Goal: Increase safety for patients receiving ICI therapy at HPH

SMART Goal: Increase safety to patient receiving ICI therapy by implementing NCCN guidelines for immune mediated adverse events and ONS patient teaching guidelines.

Objectives:

1. Implement baseline visit for patient with APRN prior to starting ICI therapy
2. Provide ICI specific education (different than chemotherapy education)
3. Provide patient with ICI identification card
4. Update ICI Beacon Protocols for baselines measures and cycle-specific measures per NCCN guidelines

SMART Objectives:

By the end of DNP project implementation (~12/15/20)

1. 80% of patients starting ICI therapy will have baseline ICI visit with APRN
2. 80% of patients receiving ICI therapy will receive education including:
 - a. Patient diagnosis
 - b. Regimen
 - c. Goals of treatment
 - d. Planned duration of treatment
 - e. Mechanism of action (MOA) of ICI
 - f. Expected response to treatment
 - g. Monitoring of irAE
 - h. When to expect side effects
 - i. When to contact cancer care team
 - j. Handling of body secretions and waste

- k. Missed appointment policy
- l. Follow up plan including labs and provider visits
- 3. 80% of patients receiving ICI therapy will be issued wallet cards
- 4. 100% of ICI Beacon protocols will have updated baseline and cycle specific lab work embedded

Process Objectives:

- 1. By February 24, 2020 literature review and synthesis completed
- 2. By March 21, 2020 meet with key stakeholders within HPH to discuss ICI project
- 3. By May 31, 2020 complete data collection for project
 - a. Chart review to assess current baseline assessment
 - b. Chart review to assess current education procedure
 - c. Chart review to establish baseline percentage of patient receiving ICI therapy with wallet cards
 - d. Beacon protocol review
- 4. By June 30, 2020 meet develop smart phrases for project
 - a. Template for baseline assessment
 - b. Template for patient education
- 5. By June 30, 2020 develop patient education packet
- 6. By July 31, 2020 meet with Beacon Team to discuss updates for ICI protocols
- 7. By August 15, 2020 train outpatient staff who will be involved in the project
 - a. APRN for review of baseline assessment
 - b. Chemo RNs for teaching

- c. Navigators/Medical Assistants (MA)/Patient Service Representative (PSR) to review project
- 8. By August 15, 2020, develop plan for obtaining wallet cards in clinic
- 9. By September 1, 2020, finalize workflow for ICI project in Straub Oncology Clinic
- 10. By September 15, 2020 start implementation of ICI program @ Straub Outpatient Oncology Clinic
 - a. Program to run September 15-December 15, 2020
- 11. By January 30, 2021, collect post implementation data to measure SMART objectives

Outcome Objectives

- 1. By January 31, 2021, the DNP student will identify additional needs within Straub Outpatient Oncology to build upon current ICI project
- 2. By January 31, 2021, the DNP student will recognize strengths and limitations of the ICI project
- 3. By December 31, 2020 Straub Outpatient Oncology will deliver evidenced based ICI care to 80% of patients receiving ICI therapy
- 4. By December 31, 2020, Straub Outpatient Oncology will document ICI care as NCCN and ONS guidelines.

Project Design

Setting

The program was implemented at Straub Medical Center (SMC) Outpatient Oncology Clinic. Straub is part of the Larger HPH, which is comprised of four medical centers-Kapiolani, Pali Momi, Straub and Wilcox. HPH is a not-for-profit health care system. As one of Hawai'i's largest health care systems, HPH provides coordinated care for maintaining health and wellness,

treating simple illnesses to complex diseases. HPH was formed in 2001 because of a merger of three long time industry leaders, Kapiolani Health, Straub Medical Center and Wilcox Health (HPH, n.d.).

Participants

The participants were adult oncology patients who started ICI therapy at the SMC Outpatient Oncology from September 15 to December 15, 2020. The number of patient participants for this project was based on the baseline chart review to estimate the average number of patients starting ICI therapy in a three-month period. Based on the number of new ICI patients, the goal was to reach 80% of these patients with appropriate teaching, baseline assessment and distribution of wallet cards.

In addition, to meeting the above objectives, the objective of 100% of ICI Beacon protocols were to have up to date baseline and lab work measures incorporated. The DNP student worked with the clinic and pharmacy staff as outlined in the Gantt chart (Appendix A).

Implementation

After baseline data was collected, materials were prepared based on the Gantt chart timeline (Appendix A). Following above, the staff were educated in regards to the new materials and proposed workflow.

The workflow to meet the SMART objectives one, two and three discussed above are as follows:

- 1) The oncologist will recommend ICI therapy for the oncology patient.
- 2) The Medical Assistant (MA) will schedule a treatment teaching with infusion nurse and a baseline assessment appointment with the APRN

- 3) The infusion nurse will educate the patient using the new materials, and addressing the 12 points outlined in SMART objective 3.
- 4) The infusion nurse will document the teaching as per 12 points outlined in SMART objective 3.
- 5) At the time of the teaching, the infusion nurse will issue the patient an ICI therapy wallet card and explain to the patient when and where this is utilized.
- 6) Prior to the start of ICI therapy, the APRN will have an office visit with the patient starting ICI and perform baseline assessment according to the NCCN guidelines Version 1.2020

The workflow to meet SMART objective four are based on the Gantt chart under Major Tasks: #3, #4 and #5 (Appendix A) and are as follows:

- 1) The ICI Beacon protocols currently in use were reviewed
- 2) NCCN guidelines for “Principles of Routine Monitoring for Immune-Checkpoint Inhibitors” were reviewed (NCCN, 2019)
- 3) A meeting was set up to discuss proposed changes with Beacon Team updates based on NCCN guidelines for “Principles of Routine Monitoring for Immune-Checkpoint Inhibitors” was discussed and approved (NCCN, 2019)
- 4) Worked with the Beacon team to update current ICI protocols NCCN guidelines for “Principles of Routine Monitoring for Immune-Checkpoint Inhibitors” (NCCN, 2019)
- 5) The Beacon team to notified the DNP student when the new ICI protocols were being developed to integrate NCCN guidelines for “Principles of Routine Monitoring for Immune-Checkpoint Inhibitors” (NCCN, 2019)

Procedures

Human Subjects Consideration

This project did not require IRB approval, as all tasks were quality improvement initiatives. Quality improvement is a process that intends to improve the processes and outcomes within a specific setting and does not produce generalizable knowledge.

The author has completed Collaborative Institutional Training Initiative (CITI) training for research ethics and compliance, and Health Insurance Portability and Accountability Act (HIPAA) training on patient privacy protections. In addition, the author has also completed HIPAA training for HPH. Based on HIPAA, all patient data collected remained confidential. Any data removed from HPH was be de-identified. All patients receiving ICI therapy was offered the same teaching intervention and baseline assessment. Any patient has the right to refuse an intervention.

Project Evaluation Plan

Measurements

Multiple methods of data collection were used to analyze this DNP ICI Project. Data collection methods consisted of quantitative measures using baseline chart reviews, post implementation chart reviews, pre and post implementation Beacon protocol review. In addition, to evaluate the sustainability of the project, outcome objectives were measured via a post implementation staff survey (Appendix B), and personnel interviews.

Data Collection Procedure

In preparation for the training and project implementation, the DNP Student determined the average monthly new ICI starts at SMC Outpatient Oncology. In addition, via ten chart reviews, the DNP student established the incidence of pre ICI therapy specific education, baseline assessment and distribution of wallet cards. Finally, ten ICI Beacon protocols were reviewed to assess if the protocol meets NCCN Guidelines Version 1.2020.

The measures for SMART objectives one, two and three after program implementation consisted of a chart review of patients who started ICI therapy during the program implementation period. For SMART objective four, the DNP student reviewed all current ICI Beacon protocols to assess if they meet NCCN Guidelines Version 1.2020.

In addition, after program implementation, a ten-item staff satisfaction survey (Appendix B) was disseminated to the staff to get feedback on the program. In addition, two personnel interviews were completed which included the nurse manager and the APRN involved in the project. These measures were intended to give staff an opportunity to give further input about the DNP ICI Project.

Data Analysis

As discussed above, after program implementation, a chart review was performed to measure SMART goals one, two and three to see the rate of adherence of the DNP ICI. This was done by data collection of charts that meet SMART goals one, two and three divided by on the number of new ICI starts during the three-month program implementation period. For SMART objective four, the total number meeting the NCCN Guidelines Version 1.2020 divided the total

number of ICI Beacon protocols. In addition, outcome objectives one and two were measured using post project interviews and a staff survey.

Results

SMART Objectives: Upon review of the charts after the implementation period, it was found that ICI specific education, wallet card distribution and baseline assessments were met at 92%. The percent of Beacon protocols meeting the NCCN guidelines was found to be 94%.

Table 1. Results Baseline and Post Implementation Chart Review

Objective	Baseline Chart Review	Post DNP Project Chart Review	% Objective Met
Rate of ICI Specific Education	0/10	12/13	92%
Rate of ICI Wallet Card Issued	0/10	12/13	92%
Percent of Baseline Assessment done	0/10	12/13	92%
% of Beacon Protocols meeting NCCN Guidelines	8/10	32/34	94%

Outcome Objectives

Staff satisfaction survey: A total of nine people completed the post DNP project survey (see Appendix D) including one MD, six infusion nurses, one nurse navigator and one medical assistant. The survey included, one background, six Likert scale, two yes/no and two opened ended questions. The survey was adapted to compensate for the inability to have a focus group during the pandemic. Eighty-nine percent (N=8) of the respondents reported they very satisfied or satisfied with the project overall, felt the project was useful, of very high or high quality, was

helpful for patients and families and planned to continue the project. Seventy-eight percent (N=7) reported that the project workflow was easy to follow (see table 2).

Interviews: Three post project interviews were completed with the APRN participating in the project, the nurse manager of Straub outpatient oncology and on oncologist. All three gave positive feedback from the program. Both the APRN and nurse manager stated that they believed that SMART objectives one two and three were being met and the program was working well for the clinic. In addition, the APRN reported feeling much better integrated with this group of patients as compared to other patients. He commented that the staff now see him as the “go to” provider for these patients. Overall, both the APRN and the nurse manager believed the care of oncology patients receiving ICI therapy was improved. The nurse manager reported that the nurses felt more guidance with giving the ICI specific education and overall process was improved. The oncologist appreciated the program and felt it to be important for safer patient care, however, had concerns about the APRN handling the increased workload.

Survey open ended questions: Questions nine and ten of the survey were opened ended questions. Question nine asked what recommendations you have to improve the DNP project, one response recommended making referring physician more aware of what the quantifiable endpoint is. Item ten in the survey asked about questions/comment or concerns about the project. Again one respondent report that they think the outcomes should have been more quantifiable and a having a control would have strengthened the project. Another respondent commented that they believed education for ICI patient was much improved which in turn will help them better recognize toxicities and aid in symptom management.

Relationship of Results to Purpose/Goals/Objectives

The purpose of the this DNP project was implement evidence based guidelines in regards to ICI therapy at Straub Outpatient Oncology with the ultimate goal of improving patient safety. It is difficult to truly measure patient safety of patients receiving ICI therapy as irAEs can occur for up to several years after ICI therapy has been complete. Furthermore, many of the patients being treated with ICI therapy have advanced cancer and will eventually succumb to their disease.

In relation to the SMART objectives one, two and three the project met the goal of 80%. SMART Objective 4 did not meet the target goal of 100%, as at the time of data collection, the Beacon Protocols that included ipilimumab still did not correct the measures to evaluate for hypopituitarism. This was discussed with the Beacon team as an ongoing recommendation and has been communicated back the DNP student that this will be corrected.

Strengths/Limitations of Project

The DNP ICI project has multiple strengths. First, as evidenced by the literature, this project highlighted an important issue in medical oncology. Patient education and monitoring of patients on ICI therapy is different from conventional chemotherapy and needs to be addressed in everyday practice. Three of four of the SMART objectives were met and the majority of the staff felt the project improved patient care and was useful. Furthermore, the clinic plans to continue using the current workflow.

Unfortunately, SMART objective four did not meet its measure on time and this ultimately a limitation. In retrospect, it would have been helpful if the DNP student reviewed the Beacon protocols prior to the final data collection and discussed earlier with the Beacon team. In

addition, it is difficult to measure the ultimate goal of this project which is to improve patient safety for patients receiving ICI therapy. Due to the scope of this DNP project as well as time allotted for project implementation this was not possible. It was obvious that one of the survey respondents also felt this was a limitation of the project, and ultimately, this may be a limitation of quality improvement projects as compared to research projects.

Sustainability

Overall, the author believes that this DNP project will be sustainable and disseminated through HPH Outpatient Oncology. HPH oncology leadership recognizes that this is an important problem in current community oncology practice that needed to be addressed. Based on the post implementation interviews and survey, the majority of the participants are pleased with the project, and plan to continue the using the materials and following the workflow. The DNP student intended to include the staff in planning and to incorporate ongoing feedback during the project, as she believed that this would help to sustain the project.

In addition, during the implementation process, the DNP student was asked by another HPH facility to implement this project at their site. The DNP student did perform an in-service and ICI project is being followed at this site. However, due the scope of the DNP project and baseline data collection, the additional site was not included in the data analysis.

Finally, recommendations will be made to HPH medical oncology operations on how to sustain the project, which will include the importance of performing in-services for each clinic prior to implementation and assuring the clinic APRNs understand how to perform the baseline assessment. Each clinic will need to have a supply of wallet cards and there will need to be a plan for updating patient education materials. Finally, it is recommended that the Beacon

protocols be reviewed annually for any changes in recommendations to lab work and assessment as immunotherapy is an evolving science and there is still data being collected on irAEs, especially in the elderly population.

Implications

The implications of this DNP project are ultimately to improve patient safety of oncology patients receiving ICI therapy through enhanced patient knowledge, tools, assessment and follow-up. As stated earlier in this paper, many academic and tertiary cancer centers now have dedicated units for immunotherapy and/or oncology urgent care clinics. Unfortunately, the community clinics do not have the resources or infrastructure to do this, but still provide oncology care to 85% of the population. Utilizing evidence-based guidelines such as ones put out by NCCN can assist these clinics in providing safe and effective care. Just as NCCN publishes guidelines on the treatment of different types of cancers, there are multiple supportive care guidelines are as important and should be followed. Managing patient side effects is paramount to providing quality cancer care. This DNP project identified a gap in the community oncology practice at HPH and worked toward improving patient care and ultimately safety to this population.

DNP Essentials

Scientific Underpinnings for Practice

Immunotherapy is a growing field in medical oncology and the need to establish safe practice cannot be understated. The extensive literature review done for this DNP project represents the importance and timely nature of this project. It also highlights the importance of nursing at both the basic and advanced level to implement safe care to oncology patients.

Organizational and Systems Leadership for Quality Improvement and Systems Thinking

This DNP project identified a population of cancer patients and oncology professionals that could benefit from a quality improvement project in regards to patients who are receiving ICI therapy. Not only did this project incorporate patients' needs, but also looked at the different needs of the clinic and staff from a multidisciplinary approach. This project was vetted among oncology administrators, oncologists, APRNs, pharmacists, nurse managers, infusion nurses, nurse navigators and medical assistants. The DNP student recognized that she needed support from all team members for this project to be a success.

This project not only assessed SMART objectives but also looked at a process and outcome objectives. It used an Implementation science framework that looked beyond the patient population, to the additional stakeholders who needed to be involved to make this project effective. This framework also kept the DNP student thinking about how this project could be sustained after the initial implementation phase.

Clinical Scholarship and Analytical Methods for Evidenced Based Practice

This project addressed implementing national guidelines for safer nursing practice and care for patients. Data collection and research findings are much more important if they are disseminated and implemented. As discussed before in this paper, this DNP project identified a gap in safe practice in a community oncology clinic and implemented evidenced-based guidelines to improve practice. Clinicians such as DNPs are needed in addition to researchers to know when and where to best apply research findings.

Information Systems/Technology and Patient Care Technology for the Improvement and Transformation of Health Care

This project worked with the information systems technology EPIC in multiple ways to implement and evaluate this project. First, a retrospective chart review was done to collect baseline and post-project implementation data on practice and Beacon protocols. EPIC was further used to implement “Smartphrases” to make templates for the APRN baseline assessment and treatment counseling, further a “Smartphrase” was made to assist the infusion RNs to document ICI specific teaching and wallet card distribution. Further, this DNP project updated all ICI specific education materials for accuracy, timeliness and appropriateness and posted them on the HPH intranet shared resources, oncology service lines portal.

Health Care Policy for Advocacy in Health Care

This DNP project addressed policy on an institutional level by addressing a need relating to quality and safety for a specific oncology population. The DNP student was able to change the patient education policy for patients receiving ICI therapy by implementing ICI specific teaching and distribution of wallet cards. Nursing assessment was also improved through the addition of the baseline ICI visit, and ongoing nursing assessment and labs references in the Beacon protocols. Educating others about the change in policy and value added by this quality improvement project is a work in progress; ongoing education to all stakeholders is planned.

Interprofessional Collaboration for Improving Patient and Population Health Outcomes

This DNP project met this DNP essential by leading multidisciplinary team throughout the project. As discussed earlier this project utilized oncology administrators, physicians, pharmacists, advance practice nurses, nurse navigators, infusion nurses and medical assistants. It

was essential to work with and see value from all these different disciplines in order for this project to be a success.

Clinical Prevention and Population Health for Improving the Nation's Health

This project aimed at improving the health of a specific cancer population by using evidenced based guidelines. By implementing these guidelines, the health of patients receiving ICI therapy at Straub outpatient oncology improved. Even though this project was not aimed at measuring health outcomes, better education and baseline data collection through the baseline assessment of this patient population ultimately improves patient safety and the quality of care.

Advanced Nursing Practice

This project met the DNP essential of advanced nursing practice in multiple areas. The lack of standard guidelines implemented for patients receiving ICI therapy was based on a comprehensive and systematic assessment of current practice within HPH system. The project was designed, implemented and evaluated based on nursing science utilizing goals and measureable objectives. The project's success was in part due to the student's professional partnerships with several key stakeholders and the relevance of the problem.

The DNP student was able to demonstrate advanced levels of clinical judgement, systems thinking and accountability in this project. She was able to guide, mentor and support other nurses participating in this project. The DNP student was able to educate and guide different members of the health care team as to why this project was of value and important to their patients. Finally, the student was able to use a conceptual framework to help guide her through this project and perform a data analysis of the projects using both quantitative and qualitative measures looking multiple types of objectives.

Conclusion

Immuno-oncology is a growing and important field within the oncology sub-specialty. Caring for patients properly with appropriate assessment, education and identification of irAEs is paramount for quality cancer care. Guidelines exist to assist clinicians in providing evidenced based care, but are not always routinely followed in practice. The DNP project was able to implement ICI evidenced based guidelines in a community oncology clinic using the DNP essentials that ultimately improved the nursing care and patient safety in the Straub Outpatient Oncology Clinic.

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Appendix A

Example of CTCAE GRADING CRITERIA FOR COMMON IMMUNOTHERAPY TOXICITIES

Symptom	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Alanine aminotransferase increased	As much as three times the ULN	3-5 times ULN	5-20 times ULN	More than 20 times ULN	–
Aspartate aminotransferase increased	As much as three times the ULN	3-5 times ULN	5-20 times ULN	More than 20 times ULN	–
Colitis	Asymptomatic, clinical or diagnostic observation only	Abdominal pain, mucus or blood in stool	Severe abdominal pain; change in bowel habits	Life-threatening consequences	Death
Diarrhea	Increase of less than four stools a day over baseline	Increase of 4-6 stools per day over baseline	Increase of seven or more stools a day over baseline; incontinence	Life-threatening consequences; hospitalization indicated	Death
Pneumonitis	Asymptomatic, clinical or diagnostic observation only	Symptomatic, limiting instrumental ADL	Sever symptoms, limiting self-care ADL, oxygen indicated	Life-threatening respiratory compromise	Death
Pruritis	Mild or localized	Intense or widespread; intermittent; skin changes from scratching; limiting instrumental ADL	Intense or widespread; constant; limiting self-care ADL or sleep	–	–
Rash (maculopapular)	Covering less than 10% of body with or without symptoms	Covering 10-30% of body with or without symptoms	Covering more than 30% of body with or without symptoms	–	–

ADL-activities of daily living, CTCAE-Common Terminology Criteria for Adverse Events; ULN-upper limit of normal

Note: *From Common Terminology Criteria for Adverse Events (v.4.03)*, by National Cancer Institute Cancer Therapy Evaluation Program, 2010.

Retrieved from: [https://evs.nci.nih.gov/ftp1/CTCAE/CTCAE_4.03/CTCAE_4.03_2010-06-](https://evs.nci.nih.gov/ftp1/CTCAE/CTCAE_4.03/CTCAE_4.03_2010-06-14_QuickReference_5x7.pdf)

14_QuickReference_5x7.pdf

Appendix B

Level of Evidence

Mosby's Level of Evidence	Evidenced reviewed
Level I: Meta-analysis, Evidenced Based Guideline	4
Level II: Evidence Obtained from at least one well designed RCT	0
Level III: Evidence obtained from one well designed controlled trial not randomized	1
Level IV: Evidence from well-designed case control or cohort studies	0
Level V: evidence from systematic reviews of descriptive and qualitative studies	15
Level VI: evidence from systematic reviews of descriptive and qualitative studies	1
Level VII: Evidence from the opinion of authorities and/or reports of expert committees	5

Appendix C

DNP ICI Project Gantt chart

Objective/Aim	Sub-Tasks	Responsible Person	Start Date	Due Date	Comments
Major Task #1: Background Project Planning					
Gather data to support project	Literature search & Synthesis	DNP student	January 2020	February 2020	
Identify Process to Implement	Review current workflow and clinic processes	DNP student	February, 1 2020	March 15, 2020	
Major Task #2: Identify Site Location					
Confirm Site of ICI Project	Need to utilize health system that has both inpatient and D/C planning home care services/community outreach	DNP Student and Content Expert	January 1, 2020	February 1 ,2020	Need to identify outpatient setting and how it will support project
	Meet with stake holders to assure project is a priority for site -Oncology leadership	DNP Student and content expert	May 1,2020	May 30,2020	Need to present project to stakeholders to assure they will buy in to project. Will need additional support besides content expert to have a successful project (adjusted due to COVID 19)
Major Task #3: Gather baseline data					
Establish incidence of baseline assessments done prior to ICI therapy that meet current NCCN guidelines	Chart review from patients starting ICI therapy in past three months	DNP Student	May 1, 2020	June 15, 2020	Important baseline data measure
Establish incidence of patient teaching for patients on ICI therapy that meet current NCCN & ONS Guidelines	Chart review from patients starting ICI therapy in past three months	DNP Student	May 1,2020	June 30, 2020	This is important to make sure you understand how DNP project will be different or can fit in with existing workflow
Establish if any wallet cards are being issued	Chart review from patients starting ICI therapy in past three months	DNP Student	May 1, 2020	May 31, 2020	

Review current ICI Beacon protocols to assess if meets NCCN guidelines	Beacon protocol review	DNP Student	May 1, 2020	June 30, 2020	Need to document baseline % of protocols meeting guidelines
Major Task #4: Develop Smart phrases and patient teaching materials					
Standardize baseline assessment	Develop smartphrase for baseline assessment based on NCCN guidelines	DNP Student	June 1, 2020	June 30, 2020	Smartphrase vs. template
Standardize patient education documentation	Develop smartphrase addressing all 12 points of patient education	DNP Student	June 1, 2020	June 30, 2020	Also need to review current ICI handouts
Standardize patient education packet	Develop packet to include handouts with appropriate readability	DNP Student	June 1, 2020	June 30, 2020	Can incorporate existing materials if appropriate Do we need funds to pay for this?
Develop plan for obtaining wallet card	Decide if ONS wallet card will be used	DNP Student, Content Expert, Nurse Manager	July 1, 2020	July 15, 2020	Need to decide which wallet card and best way to distribute-will it be paper or card-stock-do we funds to pay for this?
Major Task #4: Meet with staff involved project					
Discuss potential Beacon Protocol changes	Set up meeting with Beacon team to discuss changes to update current NCCN guidelines	DNP Student Beacon Team	June 1, 2020	July 31, 2020	Check NCCN guidelines for update version prior to meeting
Educate staff involved in project	Set up meetings with Straub Outpatient Oncology staff to introduce project, proposed changes and work flow	DNP Student , Content Expert & Nurse Manager	July 30, 2020	August 15, 2020	Need to meet with APRNs, RNs, Liaison, MA, PSR, Oncologists
Major Task #5- Implement Program					
Any new ICI treatment at Straub Outpatient Oncology gets ICI Specific teaching	Identify new ICI treatment patient-PSR can flag when scheduling treatment teach	PSR, MA, RN	September 15, 2020	December 15, 2020	Need to have treatment teach packet readily available
Any New ICI treatment patient at Straub Outpatient Oncology gets issued ICI wallet care	Need to identify where wallet card will be located	RN to distribute at treatment aching	September 15, 2020	December 15, 2020	Need to have wallet card easily accessible
Any New ICI treatment patient at Straub Outpatient Oncology get scheduled ICI baseline assessment with APRN	Need to follow up with APRN just prior to program implementation and weekly for 1 st 4 weeks to assure baseline	APRN or other provider	September 15, 2020	December 15, 2020	Need to reinforce workflow with PSR, MA, RN Navigator to assure this apt being scheduled. Ok to be same day as

	assessment is manageable				treatment start if necessary-but preferably same day as treatment teaching
`Beacon Protocols meet NCCN Guidelines	Work with Beacon team to update current protocols and set up a workflow to be notified of new protocols being developed.	Pharmacist and DNP student	9/15/20	12/15/20	Again, need to reinforce workflow for notification of new protocols being developed.
	Weekly follow up with key personnel	DNP Student	9/15/20	12/15/20	May need to adjust workflow based on feedback from staff and patients involved in project
	Major Task #6-Evaluate Program				
What is the rate of new ICI patients getting ICI specific teaching at Straub Outpatient Oncology	Gather data from chart review during implementation phase	DNP student	1/1/2021	1/31/21	Contact pharmacy-pull charts of patient starting ICI therapy 9/20-12/20/20
What is the rate of new ICI patients who have been issued wallet cards	Gather data from chart review during implementation phase	DNP student	1/1/2021	1/31/21	
What is the rate of baseline assessment being done by APRN on new ICI patients	Gather data from chart review during implementation phase	DNP Student	1/1/2021	1/31/21	
What is the rate of updated ICI protocols to meet current NCCN guidelines	Review ICI Beacon Protocols	DNP Student	1/1/2021	1/31/21	This may change with updated guidelines
Focus group	Set up meeting/focus group to allow staff to give feedback for possible change	DNP student Content expert Nurse Manager	1/15/21	1/30/21	This will also be helpful for sustainability of the project. Of note-this was not done due to COVID-19. 2 Personnel Interviews completed
Focus Group	Meet with Beacon Team	DNP student Content expert	1/15/21	1/ 31/21	This will also be helpful for sustainability of the project-of note this was changed to interviews due to COVID-19
Post Project Survey	Sent to staff	DNP student	2/1/21	2/18/21	Helpful for project sustainability and improvement
	Major Task #7-Data analysis & write up				
Data analysis	After data is gathered from above measures-	DNP student	2/1/21	2/28/21	What worked, what didn't work? Think

	DNP student, needs to further evaluate what this means-was project successful-did it meet its goals and objectives?				about recommendations for improvement
Write Paper	Write up project planning, implementation and evaluation, lessons learned and future directions	DNP student	3/1/21	3/31/21	This is probably DNP project paper but also important in overall program planning and evaluation outside the DNP project
Disseminate Data	Submit for publication	DNP Student	4/1/21	4/30/21	This may take longer based on where paper is submitted
	Discuss findings with healthcare organization	DNP student, content expert	4/1/21	4/15/21	This will be helpful to see if site wants to further implement program

Appendix D

Post DNP Immunotherapy Project Survey

1. What is your role at Straub Oncology clinic?

- ☐ Infusion nurse
- ☐ Medical Assistant
- ☐ Patient service representative
- ☐ APRN
- ☐ MD
- ☐ Other
- ☐ Other (please specify)

2. Overall, were you satisfied or dissatisfied with the DNP Immunotherapy Project?

- ☐ Very satisfied
- ☐ Satisfied
- ☐ Neither satisfied nor dissatisfied
- ☐ Dissatisfied
- ☐ Very dissatisfied

3. How useful do you feel the DNP immunotherapy project is?

- ☐ Extremely useful
- ☐ Very useful
- ☐ Somewhat useful
- ☐ Not so useful
- ☐ Not at all useful

4. How well does the DNP Immunotherapy Project meet your needs?

- ☐ A great deal
- ☐ A lot
- ☐ A moderate amount
- ☐ A little
- ☐ None at all

5. How would you rate the quality of DNP Immunotherapy Project?

- ☐ Very high quality
- ☐ High quality
- ☐ Neither high nor low quality
- ☐ Low quality
- ☐ Very low quality

6. How likely are you to continue to use the DNP Immunotherapy Project workflow/teaching materials?

- ☐ Very likely
- ☐ Likely
- ☐ Neither likely nor unlikely
- ☐ Unlikely
- ☐ Very unlikely

7. Was the DNP Immunotherapy Project workflow easy to follow?

- ☐ Yes
- ☐ No
- ☐ I don't know
- ☐ Other (please specify)

8. Do you feel the DNP Immunotherapy Project is helpful to patients/families?

- ☐ Yes
- ☐ No
- ☐ I don't know
- ☐ Other (please specify)

9. What recommendations do you have to improve the DNP Immunotherapy Project?

10. Do you have any other comments/questions or concerns related to the DNP Immunotherapy Project?

Table 2 Responses Post DNP Project Survey.

Question	N	%
What is your role at Straub Oncology clinic?		
Infusion nurse	6	66.67
Medical assistant	1	11.11
MD	1	11.11
Other: Nurse navigator	1	11.11
Overall, were you satisfied or dissatisfied with the DNP Immunotherapy Project?		
Very Satisfied	3	33.33
Satisfied	5	55.56
Neither satisfied nor dissatisfied	1	11.11
How useful do you feel the DNP immunotherapy project is?		
Extremely useful	3	33.33
Very Useful	5	55.56
Somewhat useful	1	11.11
How well does the DNP Immunotherapy Project meet your needs?		
A great deal	1	11.11
A lot	7	77.78
A little	1	11.11
How would you rate the quality of the DNP Project?		
Very high quality	2	22.22
High quality	6	66.67
Neither high nor low quality	1	11.11
How likely are you to continue to use the DNP Immunotherapy Project workflow/teaching materials?		
Very likely	4	44.44
Likely	4	44.44
Neither likely nor unlikely	1	11.11
Was the DNP Immunotherapy Project workflow easy to follow?		
Yes	7	77.78
I don't know	2	22.22