ASCO
AMERICAN SOCIETY OF CLINICAL ONCOLOGY
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Project Title: PREVIO: A Framework for Quality Improvement (QI) in Preventing Immune-Oncology Related Complications at the Ottawa Hospital

Presenter's Name: Karine Tawagi, MD GU Oncology Clinical Research Fellow

Institution: The Ottawa Hospital | The Ottawa Cancer Center

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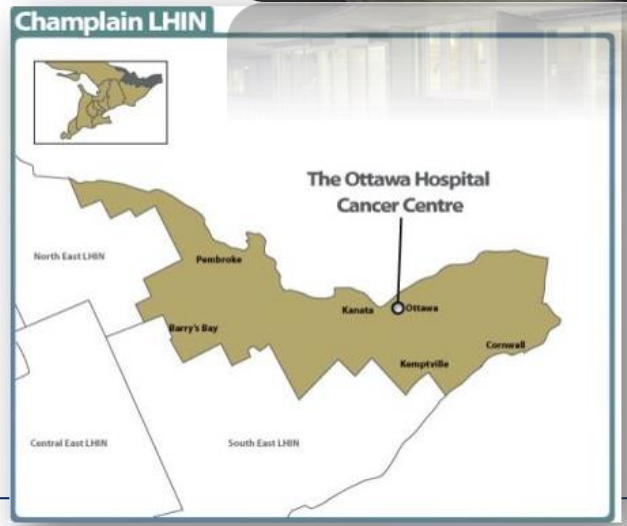
Institutional Overview

The Ottawa Cancer Center – The Ottawa Hospital

- Canada's largest academic health sciences center
- Serves a population of 1.2 million people across Ottawa, Eastern Ontario, and Nunavut
- 1,446 physicians, including >65 oncologists
- Inpatient 1,117 total beds with 56,029 admissions, and 849,471 ambulatory care visits
- >21,000 patients seen per year at TOH Cancer Center



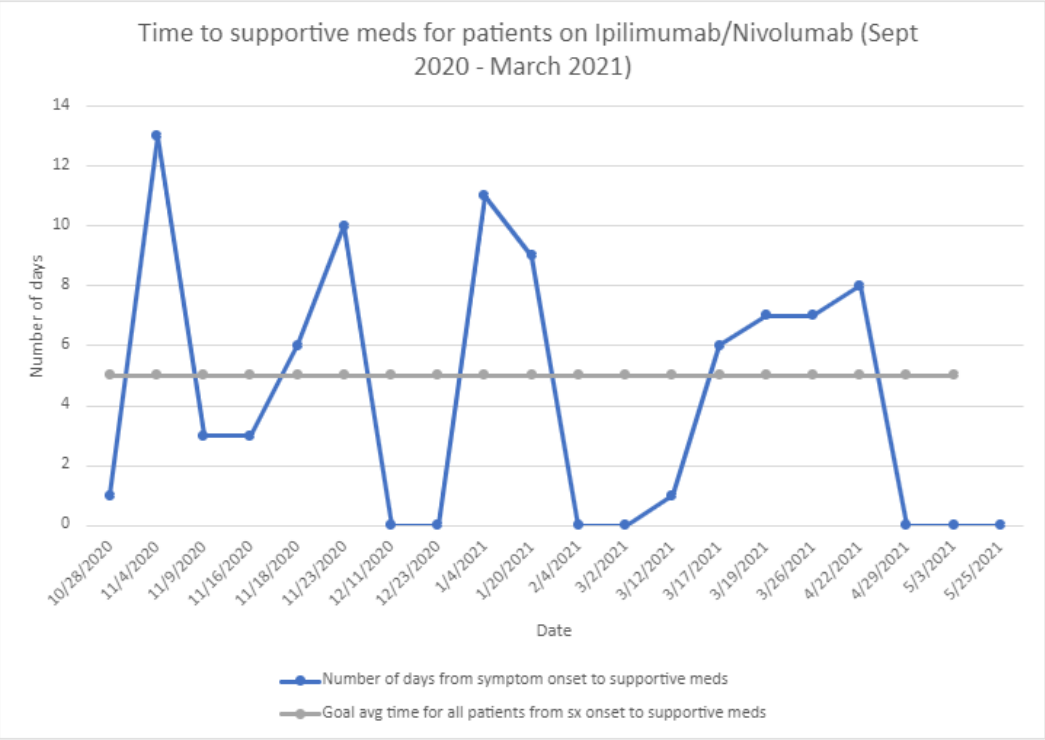
Team Members

Name	Role	Organization
Karine Tawagi, MD	Team Lead	GU Oncology Fellow, The Ottawa Hospital
Julian Surujbali, MD	Team Member	GU Oncology Fellow, The Ottawa Hospital
Michael Ong, MD	Team Member	Medical Oncologist, The Ottawa Hospital
Marcus Ward	Team Member	Process Engineer, The Ottawa Hospital
Salmaan Kanji, BsC, PharmD	Team Member	Clinical Pharmacist/Epidemiologist, The Ottawa Hospital
Shan Jin	Team Member	Methodologist, Ottawa Hospital Research Institute
Duncan Phillips, MBA	Coach	ASCO

Outcome Measure
Baseline data summary

Item	Description
Measure:	% of patients on Ipilimumab/Nivolumab who received immune-related adverse event (irAE) management compliant to ASCO guidelines, including early initiation of supportive measures
Patient Population: *(Exclusions, if any)*	Patient on Ipilimumab/Nivolumab from September 1, 2020 to March 31, 2021 at TOH
Calculation Methodology: *(i.e. numerator & denominator)*	**Numerator:** Ipilimumab/Nivolumab patients who received supportive medications within desired timeframe **Denominator:** all patients who received supportive medications while on Ipilimumab/Nivolumab
Data Source:	Epic
Data Collection Frequency:	Every 3 months
Data Limitations: *(if applicable)*	treatment plans delayed/deferred/modified, steroids given for other reasons other than irAE, unclear irAE diagnosis

Outcome Measure
Baseline data



Summary

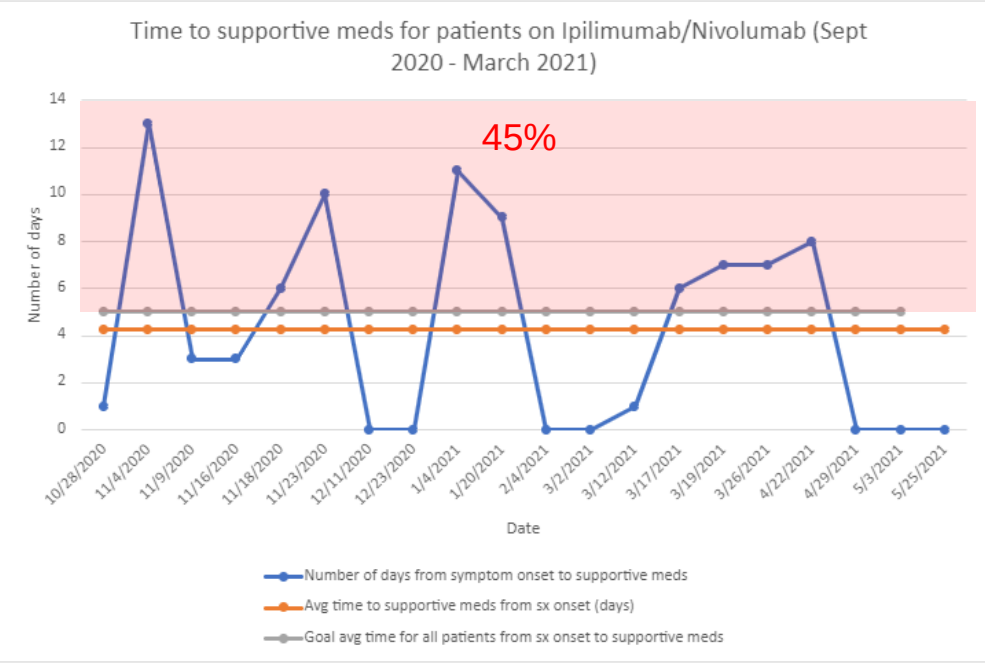
- Average = 4 days
- **All** patients should be receiving supportive medications within 5 days of symptom onset
- Targeting variability & outliers

Problem Statement

From September 2020 to March 2021…

Overall, **45%** of Ottawa Cancer Center patients on Nivolumab/Ipilimumab requiring supportive medications **did not receive these within 5 days** of symptom onset.

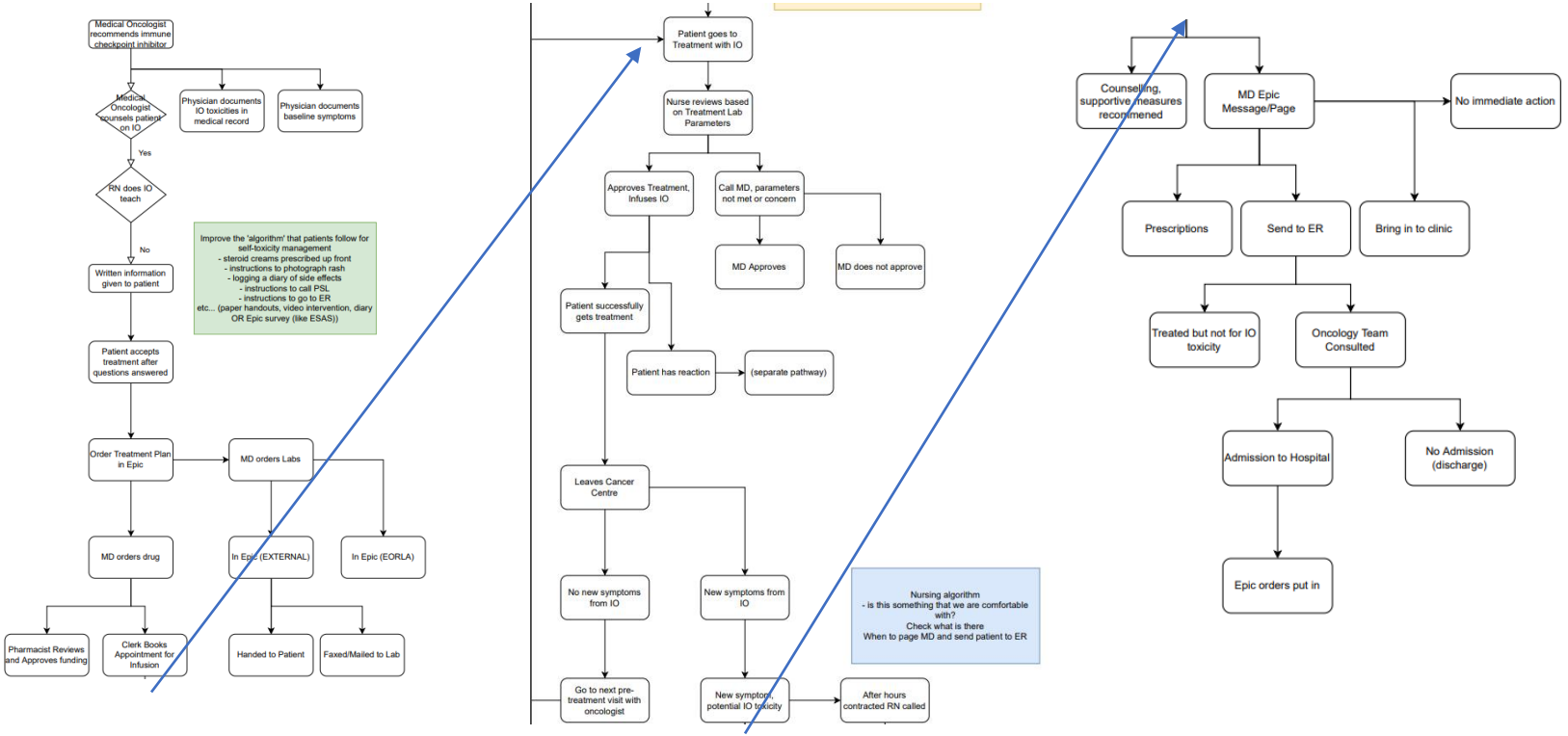
Inadequate irAE management may lead to increased ER visits, admissions, hospital LOS, premature treatment discontinuation due to toxicity, and increased morbidity/mortality for patients.



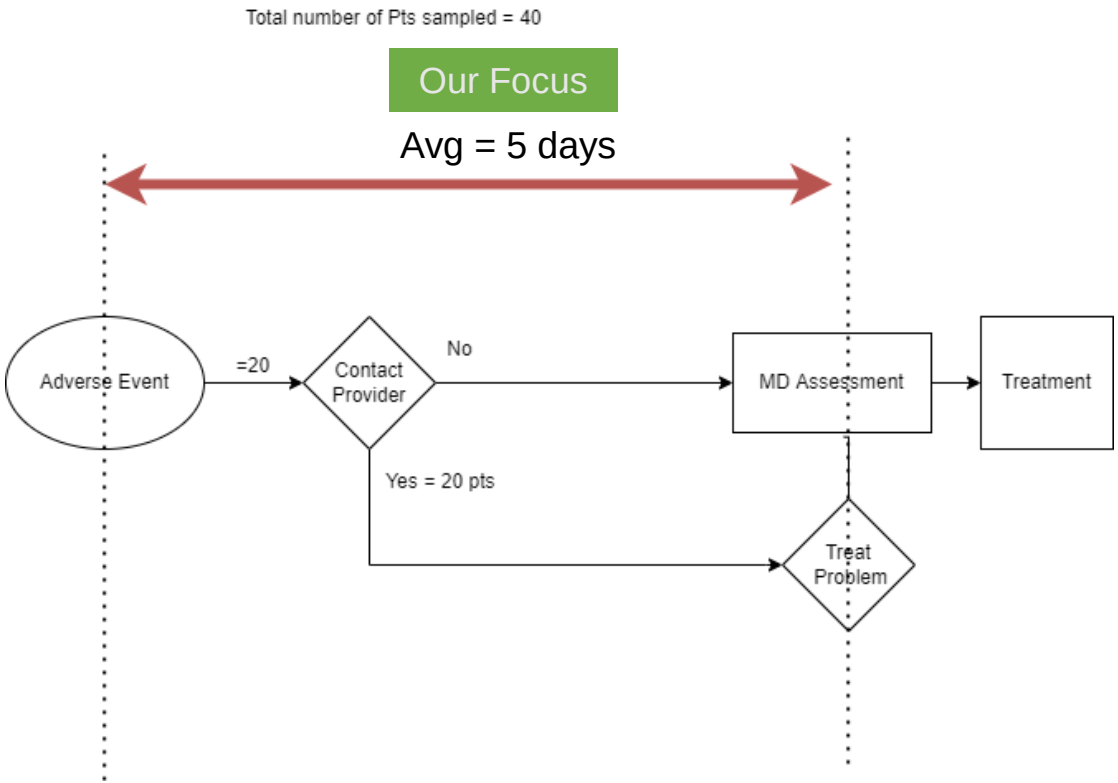
Aim Statement

Decrease the percent of Ottawa Cancer Center patients who have supportive medications for immune-related adverse events within 5 days of symptom onset from 45% to 20% by June 2021.

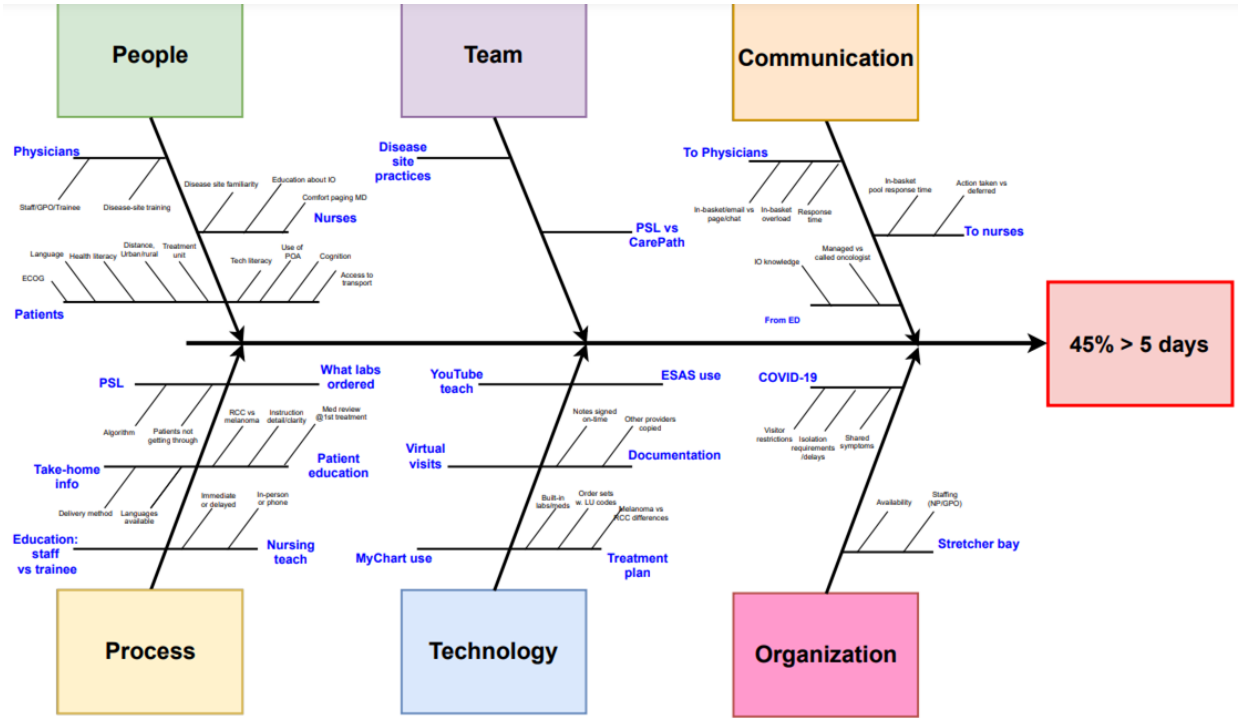
Process Map Detailed



Process Map


Total number of Pts sampled = 40
Our Focus
Avg = 5 days
Adverse Event
=20
Contact Provider
No
MD Assessment
Treatment
Yes = 20 pts
Treat Problem

Cause and Effect diagram



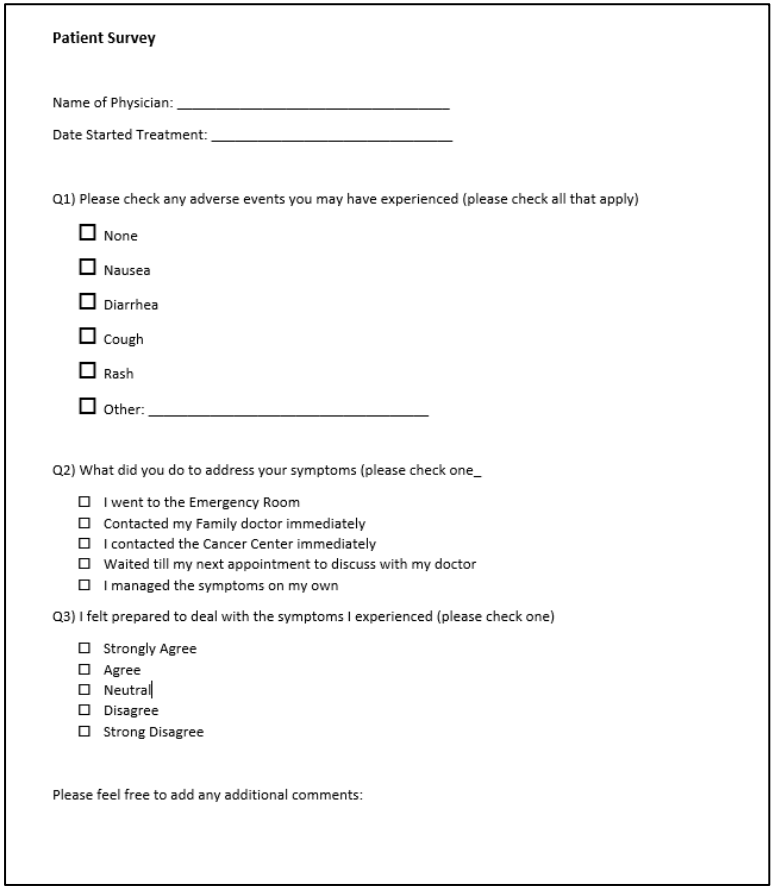
Summary

- Complex process that requires a multi-disciplinary approach
- No standardize process for managing irAEs
- Significant variability regarding the prescription of supportive medications
- **Not enough actionable information for patients**

Process Measure
Diagnostic Data summary

Item	Description
Measure:	Patient Awareness (what to do should they have an adverse event)
Patient Population: *(Exclusions, if any)*	Ottawa Cancer Center patients on Nivolumab/Ipilimumab treatment
Calculation Methodology: *(i.e. numerator & denominator)*	Completed patient survey
Data Source:	Patient Survey
Data Collection Frequency:	5-day period
Data Limitations: *(if applicable)*	Limited / small sample size

Patient Survey



Patient Survey

Name of Physician: _____

Date Started Treatment: _____

Q1) Please check any adverse events you may have experienced (please check all that apply)

- ☐ None
- ☐ Nausea
- ☐ Diarrhea
- ☐ Cough
- ☐ Rash
- ☐ Other: _____

Q2) What did you do to address your symptoms (please check one_

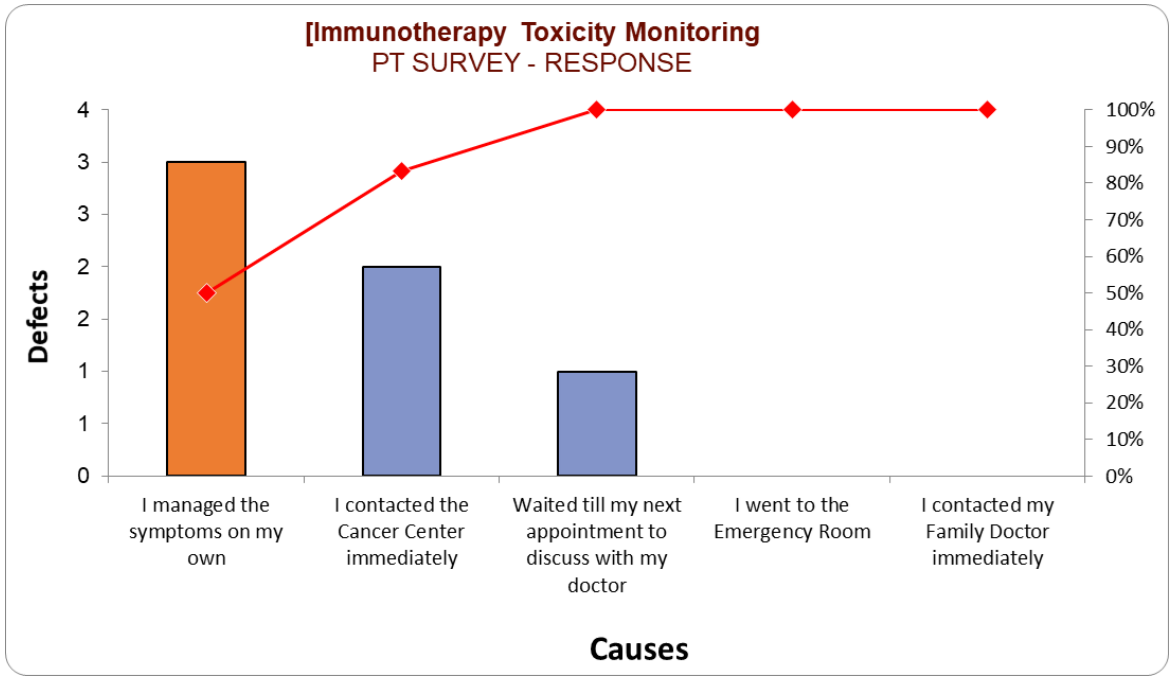
- ☐ I went to the Emergency Room
- ☐ Contacted my Family doctor immediately
- ☐ I contacted the Cancer Center immediately
- ☐ Waited till my next appointment to discuss with my doctor
- ☐ I managed the symptoms on my own

Q3) I felt prepared to deal with the symptoms I experienced (please check one)

- ☐ Strongly Agree
- ☐ Agree
- ☐ Neutral
- ☐ Disagree
- ☐ Strong Disagree

Please feel free to add any additional comments:

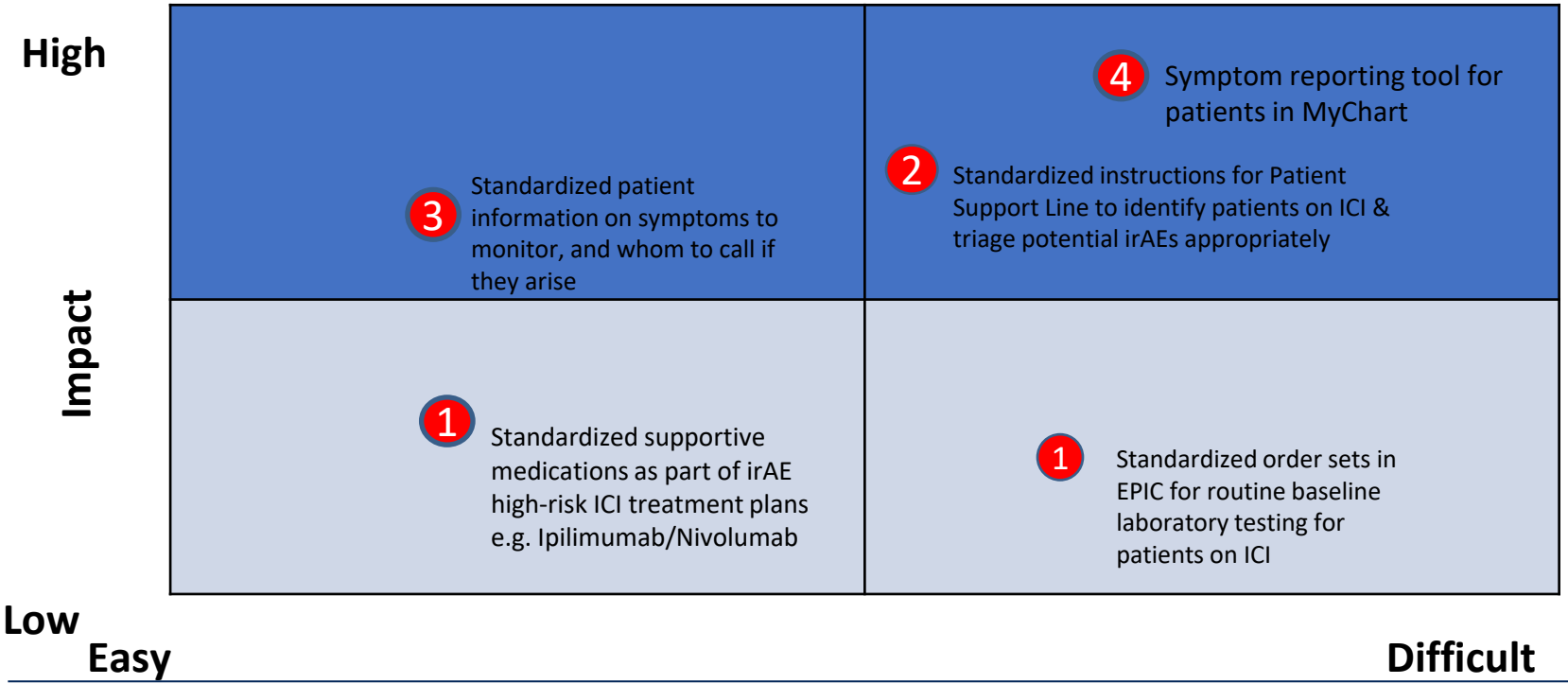
Process Measure
Diagnostic Data



Summary:

#1 response was to "manage symptoms on my own"

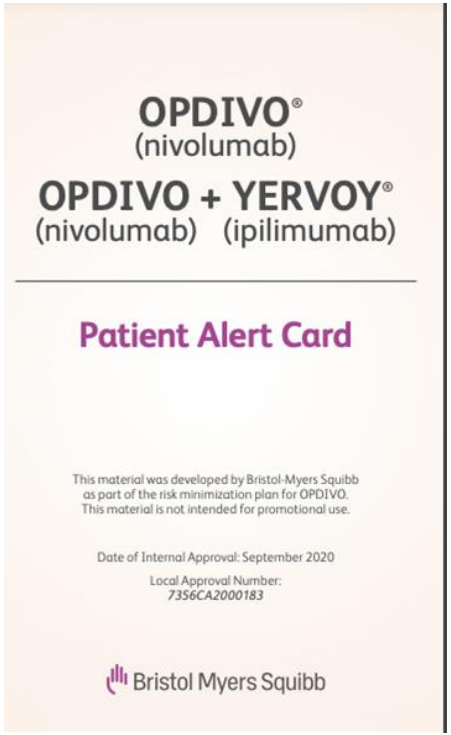
Priority / Pay-off Matrix
Countermeasures



Test of Change
PDSA Plan

Date	PDSA Description	Result
1 March 2022	Standardized order sets for patients on Ipilimumab/Nivolumab	• Discussed labs and supportive care medications to meet irAE guidelines • Met with Information Services to develop proposed changes
2 April 2022	Standardized instructions for Patient Support Line to identify patients on ICI & triage potential irAEs appropriately	• Lecture given on March 28, 2022 • Distributed to <u>all</u> nursing staff on April 20, 2022
3 April 2022	Standardized patient information on symptoms to monitor, and whom to call when they arise	• Ensure there are ICI wallet cards available, and that they are being distributed
4 2022	Symptom reporting tool for patients in MyChart	• Pending IT implementation and distribution

Wallet Patient Alert Card



OPDIVO®
(nivolumab)

OPDIVO + YERVOY®
(nivolumab) (ipilimumab)

Patient Alert Card

This material was developed by Bristol-Myers Squibb as part of the risk minimization plan for OPDIVO. This material is not intended for promotional use.

Date of Internal Approval: September 2020

Local Approval Number:
7356CA2000183

Bristol Myers Squibb

Important Information for Patients

Please carry this card with you at all times to inform healthcare professionals that you are receiving treatment with OPDIVO or OPDIVO in combination with YERVOY.

IMPORTANT

- Tell your doctor of any previous medical conditions, including if you have had a stem cell transplant that uses donor stem cells (allogeneic).
- Early assessment and management of side effects by your doctor is critical.
- Signs and symptoms that may appear mild can quickly worsen if left untreated.
- **DO NOT** try to treat these symptoms yourself.
- Signs and symptoms may be delayed and may occur weeks to months after your last injection.

For more information, consult the OPDIVO Product Monograph https://www.bms.com/assets/bms/ca/documents/productinformation/OPDIVO_EN_PIL.pdf and the Patient Information Guide or call Medical Information at 1-866-463-6267.

POSSIBLE SIDE EFFECTS

If you have any of these symptoms or any other symptoms, tell your doctor right away.

OPDIVO treatment may increase the risk of serious or even life-threatening immune-mediated side effects, which may affect different parts of the body. Signs and symptoms to look out for include the following, though these are not the only ones:

GENERAL:

- Changes in mood or behaviour (e.g., decreased sex drive, irritability, forgetfulness, depression),
- confusion and memory problems,
- feeling unwell,
- fever,
- headaches,
- increased or decreased appetite,
- nausea or vomiting,
- seizures (fits),
- seeing things that are not really there (hallucination),
- swelling in extremities,
- swollen lymph nodes,
- excessive thirst,
- hunger,
- sensation of paralysis,
- pain on the right side of your stomach (abdomen),
- tiredness,
- weight gain or loss,
- tingling and/or numbness (e.g., in your fingers or toes),
- sleepiness or drowsiness

MUSCLES AND BONES:

- Difficulty walking,
- numbness in arms and/or legs,
- muscle or joint pains,
- muscle weakness or stiffness,
- stiff neck

KIDNEYS AND BLADDER:

- Decreased or increased amount of urine,
- darker urine than normal (tea-coloured)

STOMACH AND BOWEL (GUT):

- Dark, tarry, or sticky stools,
- blood or mucous in your stools,
- diarrhea (watery, loose or soft stools) or more bowel movements than usual,
- heartburn or indigestion,
- pain or tenderness in your stomach or abdominal area

EYES:

- Eyesight changes (e.g., blurry vision, other vision problems),
- eye pain or redness,
- yellowing of the whites of your eyes

CHEST:

- Chest pain,
- breathing difficulties,
- cough,
- irregular heartbeat,
- palpitations (being more aware of heartbeat than normal)

MOUTH, NOSE AND THROAT:

- Ulcers in the mouth or other mucous membranes

SKIN:

- Bruising easily,
- dry skin,
- itching,
- raised skin lumps/bumps (skin nodules),
- severe skin reaction or rash,
- skin blistering/peeling,
- skin yellowing (jaundice)

IMPORTANT information for healthcare professionals

- This patient is treated with **OPDIVO** or **OPDIVO in combination with YERVOY**.
- Immune-mediated adverse reactions (imARs) may appear at any time during treatment or months after its discontinuation.
- Early diagnosis and appropriate management are essential to minimize life-threatening complications.
- Consultation with an oncologist or other medical specialist may be helpful for management of organ-specific imARs.

Consult the OPDIVO Product Monograph at https://www.bms.com/assets/bms/ca/documents/productmonograph/OPDIVO_EN_PM.pdf

or call Medical Information at 1-866-463-6267 for more information.

Reporting side effects

You can report any suspected side effects associated with the use of Health Products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Reference: 1. OPDIVO Product Monograph. Bristol-Myers Squibb Canada, August 6, 2020.

My Doctor's Contact Information

(who prescribed OPDIVO or OPDIVO in combination with YERVOY)

Name of Doctor: _____

Office Phone: _____

After-Hours Phone: _____

The healthcare professional treating this patient with OPDIVO or OPDIVO in combination with YERVOY should complete the 'My doctor's contact information' section of this Patient Alert Card.

My Contact Information

My Name and Phone Number: _____

Emergency Contact (name and phone): _____

PATIENT SUPPORT LINE: IMMUNE-TOXICITIES CHEAT SHEET

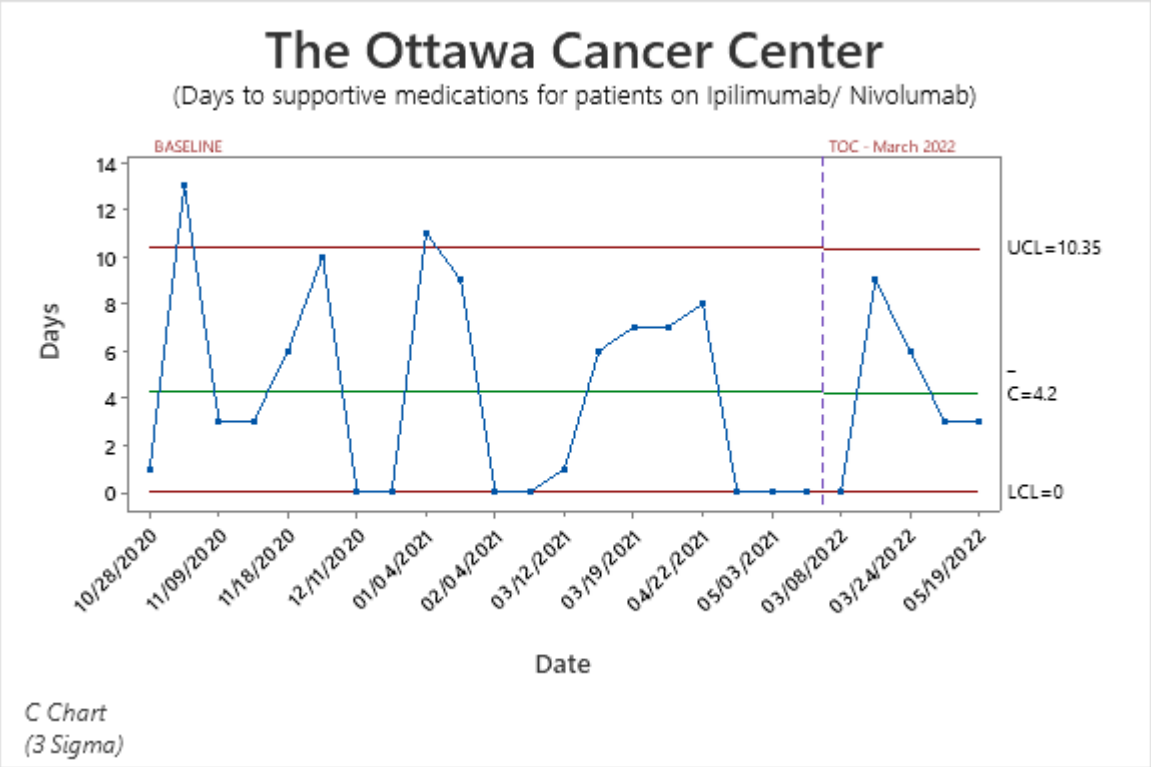
There are different classes of immunotherapy:
Anti-PD1/PDL1: Pembrolizumab, Nivolumab, Cemiplimab, Durvalumab, Avelumab, Atezolizumab, Dostarlimab
Anti-CTLA4*: Ipilimumab or Tremelimumab (*higher-risk of side effects)

Toxicities can affect ANY organ – EARLIER intervention prevents hospitalization/death **Disclaimer this is a meant to be used as a guide, other medical issues outside of toxicity to immune therapy can occur

MUCH higher risk of toxicities on combined IPILIMUMAB + NIVOLUMAB
- **Very low threshold to notify MRP even with mild symptoms.**
- **No side effects from immunotherapy are 'normal' or 'expected' (they are autoimmune)**

1. **Diarrhea / Colitis** – *common, ranges from mild to very serious*
    a. **For mild diarrhea, 1-3 diarrheal movements/day, no abdo pain or blood/mucous:**
        i. Imodium/loperamide 4mg then 2mg Q4H until diarrhea free for 12 hours (max 16mg daily) by prescription (LU code 113; prescribed by MD)
        ii. Dietary counselling – avoid dairy products (CTLA-4 -> lactose intolerance), ensuring they are getting enough fluids, avoiding greasy/spicy/fried foods and alcohol/caffeine, eating small meals.
    b. **For moderate-severe diarrhea 4 or more diarrheal movements/day OR new abdominal pain or blood or mucous in stool (signs of colitis):**
        i. **Page MRP MD & book into clinic**
        ii. **Discuss with MD if DIRECT TO ER to see Med Onc team**

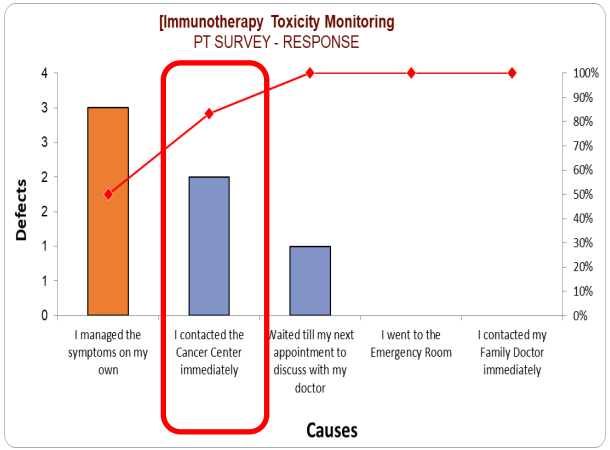
Outcome Data

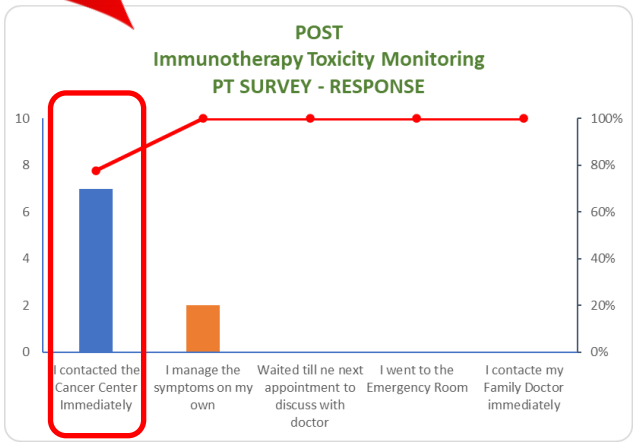


Summary

- 23 more patients were identified who received any of cycle 1 through 4 Ipi/Nivo in 2022, 7 of these patients required supportive medications for symptoms related to treatment
- Still variability but perhaps progress towards <5 day metric from symptom onset to supportive medications

Before & After





Summary

BEFORE:
"I contacted the Cancer Center" = 2

AFTER:
"I contacted the Cancer Center" = 7

Patient Survey responses

If you have new symptoms while on your immunotherapy treatment, what will you do/who will you contact?

- (60F): *depends, if mild, would call GP first since closer, if more severe would call my sister (doesn't have access to long distance calling) who would then call patient support line (PSL) on her behalf*
- (87M): *if severe - would call PSL, if mild - may manage on own; not that easy to get someone on line for PSL (thought # was on wallet card but it wasn't), would go to ED if couldn't reach someone*
- (85M): *had diarrhea for 5-6 days up to 7-8BM at its worse, didn't do anything because thought it would improve*
- (62M): *no side effects so far but for example, if had 5 episodes of diarrhea tomorrow, would change diet, eat bananas, strawberries, rice, make it solid. Would not call unless really severe. Was not aware could get adverse events at any time.*

Next Steps/ PDSAs

Next Steps	Owner
Expand patient education	Karine Tawagi
Develop RN follow-up process	Karine Tawagi
Develop Registry database	Karine Tawagi
CAMIO Conference: **Canadian Advances in Managing Immuno-Oncology** Multi-disciplinary conference to establish irAE best practices (Sept 30, 2022)	Michael Ong

Conclusion

- Ongoing data collection is required to determine if there is a trend after our tests of change
- irAES are complex, having routine follow-up patient education would be helpful
- Continuing to establish best practices which can be measured with prospective registry of all patients on immunotherapy, both combination and monotherapy regimens