Immune Checkpoint Inhibitor-Associated Primary Adrenal Insufficiency
SBAR 6/15/2022

Recommendation: Monitor morning blood cortisol levels at baseline and prior to surgery in neoadjuvant treatment plans that contain ICI.

Situation
During the Keynote-522 trial, a patient died of adrenal crisis one day after surgery. There is concern that patients may develop primary adrenal insufficiency (PAI) from immune checkpoint inhibitor (ICI) therapy and not be diagnosed prior to surgery, which can result in significant morbidity and mortality.

Background
As a result of the fatality in the Keynote-522 trial, Merck added the following to the package insert for pembrolizumab "For patients with triple negative breast cancer (TNBC) treated with KEYTRUDA in the neoadjuvant setting, monitor blood cortisol at baseline, prior to surgery, and as clinically indicated.”

Based on a meta-analysis published in 2020, the rate of primary adrenal insufficiency with immune checkpoint inhibitors is 0.001%-0.01% of immune related adverse events. Up until this meta-analysis, this adverse event is only described in various case reports due to such a low incidence. Currently, we do not monitor for PAI other than physician monitoring for symptoms, which include asthenia, nausea, vomiting, and low blood pressure. These clinical symptoms are non-specific, which increases a patient’s risk of having PAI and not being diagnosed and treated. Furthermore, we currently do not perform any laboratory monitoring, such as blood cortisol levels, in patients on ICI. Recently published trial in NSCLC had an incidence of 2 patients (1.1%) with adrenal insufficiency. No deaths reported from adrenal insufficiency.

Cortisol levels drawn prior to 9am are the most accurate and can aid physicians in identifying patients with PAI.

Assessment
Patients who go to surgery are at highest risk of morbidity and mortality from untreated PAI. To adequately monitor patients with TNBC on pembrolizumab + chemotherapy, we should draw morning blood cortisol levels (prior to 9am).

Recommendation
Draw morning blood cortisol levels (prior to 9am) at baseline and 1-2 weeks after last dose of immune checkpoint inhibitor prior to surgery. Patients will need to be scheduled for labs no later than 8am. These details will be in the order in the treatment plan for pembrolizumab + chemo in TNBC and other neoadjuvant treatment plans that contain an ICI.

Approval
OPN: 06/09/2022
Communication Plan
Education will need to be provided to outpatient infusion nurses, pharmacists, and potentially scheduling teams.

Applicable to:
☐ CSC Infusion  ☐ Ridges Infusion  ☐ Southdale Infusion  ☐ Maple Grove Infusion  ☐ Other  ☒ System

References: