Hello everyone my name is Lisa Cordes andIm an oncology clinical pharmacy specialist

I am happy to be here with you today to discussthe case of a young woman with renal cell carcinoma whos currently being treated withan immunotherapy regimen

As Dr Gulley discussed in his presentationsimmunotherapies have really revolutionized the treatment of our patients with cancer

More patients are responding to treatmentstheir responses are durable and theyre really living longer

However with immunotherapies comes autoimmunetoxicities that require a completely different treatment approach than toxicities seen withour traditional cytotoxic chemotherapy

So why do autoimmune toxicities occur withimmunotherapeutic agents?

So Dr Gulley went over this in his slidesso Im only going to highlight a few important points

Selftolerance is partially maintained bythe inhibition of T cells in the CTLA and PDPDL pathways

So if we inhibit these pathways by using drugssuch as ipilimumab which inhibits the CTLA pathway or nivolumab which inhibits thePD pathway that unleashes the T cells and that leads to the potential for autoimmunity

Whats interesting about these toxicitiesis that any organ system can be involved

so that can be the dermatologic system itcan be cardiac it can be the neuro system

really no system is safe and so its importantto counsel your patients to be on the lookout for toxicities that occur with any of theseorgan systems

Also the onset is variable so you can giveone patient one dose of an immunotherapy and it can cause an autoimmune toxicity or itcan be months and months after theyve stopped the treatment and then at that time they couldhave the toxicity

So our patient Rebecca [spelled phonetically]is a young an otherwise healthy female with

metastatic renal cell carcinoma

At this time shes received three doses ofipilimumab and nivolumab and she was just admitted to the hospital

Rebecca is meeting with her oncologist DrRedman [spelled phonetically] right now

Lets listen in

Male Speaker:Hawaii Rebecca Im sorry to hear youre not feeling that well

Whats been going on?

Female Speaker:The past few days havent been very good

I started having really bad diarrhea I haveto go to the bathroom about 0 times a day when I usually only go once

I also have severe abdominal cramping itfeels like someone is twisting my intestines

Male Speaker:Im sorry to hear that

Looking at your blood pressure its a littlelow and your labs show me that youre a little dehydrated

I think this is all due to an inflammatoryprocess in your colon and we can treat it with steroids but Id like to admit you justto get treatment started

Lisa Cordes:Okay so lets pause for a second

What grade of colitis is Rebecca currentlyexperiencing?

For grading we reach to something calledthe CTCAE

This was put together by the National CancerInstitute and its a common terminology criteria for adverse events

Essentially what this is is a descriptiveterminology that allows us to commonly assess adverse events that our patients are experiencingand name them in the same way

So as Dr Redman mentioned her workup revealedan inflammatory process in her colon which means she has colitis

So we go to our CTCAE term for colitis andwe see that its graded on a scale of Grade

which is minimal toxicity all the wayto Grade which is patient death

So as Rebecca mentioned she has severe abdominalpain so if you look down you can see that

is a Grade toxicity

So once youve determined the grade of theadverse event you can then use the treatment

guidelines to determine the next best treatmentstrategy

There are multiple different treatment guidelinesavailable for autoimmune toxicities and theyre

listed here for you

We have ASCO ESMO SITC

We also have NCCN or the National Cancer ComprehensiveNetwork and they have the management of immunotherap

related toxicities and were just going tohighlight them for an example today

As you can see here is our initial treatmentstrategy for colitis and Rebecca has a severe

toxicity which means she has a Grade or toxicity

First were going to hold the immunotherapyregimen and not give it until we figure out

whats going on

We can consider inpatient care in Rebeccascase she was admitted to the hospital for

supportive care

So we want to give her some hydration becauseshe was dehydrated and we also want to correct

her electrolyte imbalances to better carefor her

Well also start steroids as Dr Redman mentioned

The recommendation for a severe colitis isIV methylprednisolone at a dose of milligram

per kilogram once every day

So as we mentioned the patient was startedon the steroid dose and the oncologist is

rounding on her now

So lets see how shes doing

Male Speaker:So youve been on steroids for about two

days now are you feeling any better?

Female Speaker:Honestly I dont think its gotten better

I still have persistent cramping

Lisa Cordes:So as youve heard Rebeccas colitis has

not improved

She still has a lot of symptoms

So now we think okay what is the next beststep in managing this adverse event

So again we go back to our NCCN treatmentguidelines and we look for steroidrefractory

treatments and so as you can see if theresno response to the steroids that we initiated

within two days we want to look for anothertreatment option

So here were going to continue the steroidsbut were going to add an agent called infliximab

Infliximab is an agent thats FDA approvedfor different types of autoimmune diseases

such as Chrons disease and different typesof arthritis and it inhibits something called

tumor necrosis factor alpha

Essentially TNF alpha is involved with proinflammatorybiologic activities

So what were going to do is were goingto use the infliximab come in and inhibit

TNF alpha and thats going to inhibit theinflammatory process thats currently going

on

So as we recommended infliximab was addedto Rebeccas regimen and her symptoms quickly

improved

So at this time the methylprednisolone canbe transitioned to an oral prednisone regimen

and then tapered over about to weeks

We taper over a long period of time so thatthe symptoms dont flare

If you taper too quickly we actually mightsee a recurrence in her symptoms

So while shes on the steroids dont forgetabout whether we need PCP prophylaxis fungal

prophylaxis or a proton pump inhibitor

Patients like Rebecca are seen every day inour clinic and we hope this case provides you with some insight into her treatment strategyfor autoimmune toxicities

We do recommend that you refer to the treatmentguidelines and prescribing information for further details on both the diagnosis andthe management of these unique toxicities

Thanks so much for watching