

YOUR OPDIVO[®] (nivolumab) ACTION PLAN

(to be filled out by a member of your oncology team)

For Kidney Cancer (Renal Cell Carcinoma)

Patient Name		_ Date	
	Full Name		Today's Date
Side effects discussed			
Key points			





TAKING THE MEDICATION OPDIVO® (nivolumab)

HOW IT'S GIVEN:

- Opdivo is given through your vein via an intravenous (IV) line. The treatment usually takes 30 minutes but can take 60 minutes
- · Opdivo is usually given every 2 or 4 weeks, depending on the indication
- · Your consultant will decide how many treatments you need
- · You will need to have blood tests before, during, and after treatment
- It is important to keep appointments with your healthcare team to receive your treatment. If you miss an appointment, call
 as soon as possible to reschedule and to receive instructions about what to do

Problems you may have while receiving the medications through the IV line: Some people may have a bad reaction to the IV treatment itself. Tell your consultant immediately if you have any of these symptoms during a treatment session:

Chills or shaking

· Itching or rash

· Difficulty breathing

 Feeling like you are going to pass out

- Flushing (turning red)
- Dizziness
- Fever or feeling hot

Common side effects of Opdivo: Even minor side effects could be serious and you should report them all to your consultant. The most common side effects of taking Opdivo are:

- Pain in muscles, bones, and joints
- Diarrhoea
- Cough
- Constipation
- Back pain
- Fever
- Rash

- Itchy skin
 - Nausea
 - Shortness of breath
 - · Lack of interest in food
- Upper respiratory
 infections (colds and flus)
- Weakness

how you feel to your consultant:

Report any changes in

Even small changes in your health or the way you feel that don't seem like a big deal may be a sign of a serious side effect. Don't "tough it out" or try to manage it yourself if you think you are having a side effect—report it immediately! Getting it checked out early may prevent it from becoming a bigger problem.

Avoid pregnancy: Use birth control during therapy and for 3 months after your last treatment if you are of childbearing age. Tell your consultant right away if you or your partner becomes pregnant or think you are pregnant while on Opdivo as it can cause harm to an unborn baby.

IMPORTANT SIDE EFFECTS

Your consultant may discuss some side effects of Opdivo that can lead to serious problems if they aren't taken care of right away. These sections give information about possible symptoms, what you should tell your consultant, when you should get medical help immediately, and any steps you can take to help ease the symptoms.



LUNG AND BREATHING PROBLEMS

OPDIVO[®] (nivolumab)

Report immediately to your consultant's office

What are the symptoms?

- Changes in breathing
- Worsening of existing breathing symptoms
- Increased shortness of breath when you walk or exercise
- Shortness of breath when you are resting

- Dry cough • Chest pain
- What you should tell your consultant:
 - When you first noticed the changes in your breathing or cough
 - If you are feeling very tired, are wheezing (making a whistling sound when you breathe), or have a fever
 - · If the symptoms are interfering with your daily activities
 - If you've ever had breathing problems before and if your existing symptoms are worse
 - If you have respiratory allergies to pollen, trees, pets, or other things or food allergies and if you've recently been exposed to these allergens
 - If you think you've been exposed to cold or flu viruses
 - Interventions you've tried at home (eg, inhaler, cough medicine, etc)

Red flag(s):

- For severe symptoms, call for an ambulance immediately and inform Acute Oncology service/on-call triage in the treating hospital
- For less severe symptoms, call Acute Oncology service/on-call triage in the treating hospital for instructions or go to the accident and emergency (A&E) department at the local hospital

Regardless of where you are being treated, be sure to inform the treating healthcare professional (HCP) that you are receiving immunotherapy and show them the documentation (eg, wallet card for your medication)

Taking care of your lungs:

- Avoid environments that can irritate your lungs or make it hard to breathe. For instance, if you work outdoors, pollen or chemicals may affect you. If you have a hobby like painting, use of certain chemicals might be a problem
- Wear a pollen mask or a respirator when you are around things that may irritate your lungs
- Adhere to any pre-existing asthma or allergy treatment plans during your cancer therapy
- Check with your healthcare professional before using any steroid-based inhalers



DIARRHOEA/STOMACH PROBLEMS OPDIVO® (nivolumab)

Report immediately to your consultant's office

What are the symptoms?

- Diarrhoea or mushy poo
- Changes in your bowel movements (more or less frequent)
- Nausea (upset stomach) and vomiting (throwing up)
- Bloating in the stomach and/or gas
- Feeling very tired
 Fever

- Pain or cramping in the stomach
- Lack of interest in food

What you should tell your consultant:

- When you first noticed the changes in your bowel movements
- What your bowel movements are like-hard, solid, soft, loose, or liquid
- What colour your poo is-light or dark-and if there is blood or mucus in it
- · If your poo floats
- · How often you are having bowel movements
- If you have any of the other symptoms listed in the box above
- If you have been losing or gaining weight without trying
- · How much and what you are eating and drinking each day
- If you've ever had digestive/stomach problems before
- · If the symptoms are interfering with your daily activities
- A list of medications and supplements you're taking
- Anything else you have tried at home to manage the symptoms

Red flag(s):

- For severe symptoms, call for an ambulance immediately and inform Acute Oncology service/on-call triage in the treating hospital
- For less severe symptoms, call Acute Oncology service/on-call triage in the treating hospital for instructions or go to the accident and emergency (A&E) department at the local hospital

Regardless of where you are being treated, be sure to inform the treating healthcare professional (HCP) that you are receiving immunotherapy and show them the documentation (eg, wallet card for your medication)

Taking care of your digestive system:

- Call your consultant or the ward where you are treated IMMEDIATELY if you have diarrhoea
- Take over-the-counter or prescription medications AS INSTRUCTED by your consultant
- Avoid spicy foods, high-fibre cereals, red meats, fats, dairy products, raw fruits (except bananas), vegetables, caffeine, alcohol, and sugar
- Instead, eat bland foods such as bananas, rice, toast, oatmeal, or crackers
- Drink water, weak tea, clear broth, watered-down juice, Dioralyte[®], or isotonic sport drinks (Lucozade[®], Powerade[®]), or suck on ice pops to prevent dehydration
- Do not use laxatives or poo softeners if you have diarrhoea
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KIDNEY PROBLEMS OPDIVO[®] (nivolumab)

Report immediately to your consultant's office

What are the symptoms?

- Changes in how often you urinate
- Changes in the colour of your urine, blood in your urine
- Pain or hesitation when you urinate
- Pain in your upper back or belly and sides (flank pain)

What you should tell your consultant:

- When you first noticed the changes in urination and if the changes came on slowly or suddenly
- What the colour of your urine is (light, dark) and whether you've noticed blood in it
- If your urine is foamy or bubbly
- · How often you are urinating (more or less frequently)
- · If you are having any trouble urinating
- How much and what you are drinking each day
- If you have pain in your lower stomach or back:
 - Sharp or dull
 - Constant or it comes and goes
- If you also have nausea or vomiting (throwing up)
- If you have a headache and/or a general feeling of being unwell
- If you have swelling in your ankles
- If you have a fever
- If you have lost your appetite
- If you've ever had urinary tract infections or kidney problems before
- If the symptoms are interfering with your daily activities
- · A list of medications and supplements you're taking
- · Anything else you have tried at home to manage the symptoms

Red flag(s):

- For severe symptoms, call for an ambulance immediately and inform Acute Oncology service/on-call triage in the treating hospital
- For less severe symptoms, call Acute Oncology service/on-call triage in the treating hospital for instructions or go to the accident and emergency (A&E) department at the local hospital

Regardless of where you are being treated, be sure to inform the treating healthcare professional (HCP) that you are receiving immunotherapy and show them the documentation (eg, wallet card for your medication)

Taking care of your kidneys:

- · Drink lots of fluids every day to flush your system out
- Avoid alcohol and caffeine
- Check with your healthcare professional (HCP) before taking any non-steroidal anti-inflammatory drugs (NSAIDs) such as aspirin and ibuprofen



SKIN CHANGES OPDIVO® (nivolumab)

Report immediately to your consultant's office

What are the symptoms?

- A skin rash with or without itching
- Skin burning or tightness
- Itching without a rash

- Skin blisters
- Peeling skin
- Sores in your mouth or rectum

What you should tell your consultant:

- . When you first noticed the rash or itchiness
- What the rash looks like (eg, flat, bumpy, red, acne-like, nettle rash)
- Where the rash is and how much of the body it is covering
- If the skin change is making it difficult for you to get dressed, perform daily activities, or sleep
- If you have had any skin problems in the past
- · If you have started any new medications recently
- If you have been using a new soap or been around new chemicals or animals recently
- · What you have tried at home to manage the symptoms

Red flag(s):

- For severe symptoms, call for an ambulance immediately and inform Acute Oncology service/on-call triage in the treating hospital
- For less severe symptoms, call Acute Oncology service/on-call triage in the treating hospital for instructions or go to the accident and emergency (A&E) department at the local hospital

Regardless of where you are being treated, be sure to inform the treating healthcare professional (HCP) that you are receiving immunotherapy and show them the documentation (eg, wallet card for your medication)

Taking care of your skin:

- Avoid soap. Instead, use gentle, non-soap cleansers such as Cetaphil®
- Avoid hot showers or baths (short, lukewarm showers are OK)
- Apply a cool cloth to the area
- Apply a cooling cream with menthol or camphor to the area (refrigerate the cream first for even greater relief)
- · Keep your fingernails short to protect your skin from damage if you scratch
- Apply a moisturiser that contains the ingredients urea or glycerine daily
- Don't use lotions that have perfumes or dyes
- Protect your skin from the sun by wearing sunscreen, a hat, and UV-protective clothing and sunglasses. Don't forget your hands and face
- Your consultant may tell you to take an antihistamine by mouth or apply a hydrocortisone cream to reduce the itching



MOUTH PROBLEMS OPDIVO[®] (nivolumab)

Report immediately to your consultant's office

What are the symptoms?

- Sensitivity or burning when you eat/drink
- Mouth sores

• Dry mouth, dry or thick saliva

• Mouth pain affecting your tongue, gums, and the inner lining of the cheeks and lips

What you should tell your consultant:

- When you first noticed the changes in your mouth
- If the changes are making it difficult for you to eat, drink, or swallow
- If you have been losing or gaining weight without trying
- · If you are waking up at night to sip water
- If your symptoms are worsening
- Any mouth or dental problems you have had in the past and how severe they were
- · How much and what you are drinking each day
- · A list of medications and supplements you're taking
- · If you are using any lozenges for dry mouth
- Anything else you have tried at home to manage the symptoms

Red flag(s):

- For severe symptoms, call for an ambulance immediately and inform Acute Oncology service/on-call triage in the treating hospital
- For less severe symptoms, call Acute Oncology service/on-call triage in the treating hospital for instructions or go to the accident and emergency (A&E) department at the local hospital

Regardless of where you are being treated, be sure to inform the treating healthcare professional (HCP) that you are receiving immunotherapy and show them the documentation (eg, wallet card for your medication)

Taking care of your mouth:

- Drink lots of fluids every day
- Avoid hot, spicy, or acidic foods (such as tomatoes)
- Brush your teeth at least twice a day using a soft toothbrush. Avoid toothpaste with whitening agents
- Floss once a day
- Use mouth rinses, mints, or other products recommended by your consultant to relieve your mouth symptoms
- Avoid commercial mouthwashes or those that have alcohol in them as they can dry your mouth out more
- · Have regular dental check-ups
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LIVER PROBLEMS OPDIVO[®] (nivolumab)

Report immediately to your consultant's office

What are the symptoms?

- Changes in your energy level (more tired)
- Yellowing of your skin or the whites of your eyes
- Change in the colour of your poo (paler)
- Change in the colour of your urine (darker, tea-coloured)
- Abdominal pain, particularly on the upper right side of the stomach
- Bruising more easily
- Bleeding more easily
- Fever
- Confusion, drowsiness, feeling "foggy"
- Increased sweating
- Abdominal bloating

What you should tell your consultant:

- · When you first noticed the symptoms above
- · How severe the symptoms are
- If you have been losing or gaining weight without trying
- If the symptoms are interfering with your daily activities
- A list of medications and supplements you're taking (especially any product containing acetaminophen [example, paracetamol])
- If you drink alcohol and how much per day
- If you've ever had liver problems before
- · Anything else you have tried at home to manage the symptoms

Red flag(s):

- For severe symptoms, call for an ambulance immediately and inform Acute Oncology service/on-call triage in the treating hospital
- For less severe symptoms, call Acute Oncology service/on-call triage in the treating hospital for instructions or go to the accident and emergency (A&E) department at the local hospital

Regardless of where you are being treated, be sure to inform the treating healthcare professional (HCP) that you are receiving immunotherapy and show them the documentation (eg, wallet card for your medication)

Taking care of your liver:

- Drink lots of fluids every day
- Don't drink a lot of alcohol (no more than one drink per day for women and two drinks per day for men) or avoid alcohol all together
- Eat a well-balanced diet without too much fat and stay active to maintain a healthy weight
- Do not take more acetaminophen (example, paracetamol) or prescription pain medication than recommended



PITUITARY GLAND PROBLEMS

OPDIVO[®] (nivolumab)

Report immediately to your consultant's office

What are the symptoms?

- Changes in your energy level (more tired)
- Dizziness
- Nausea/vomiting
- Headache

- Confusion, drowsiness, feeling "foggy"
- Problems with your vision
- Changes in sexual function

• Fever

What you should tell your consultant:

- When you first noticed the symptoms above
- · How severe the symptoms are
- · If the symptoms are interfering with your daily activities
- · A list of medications and supplements you're taking
- · If you've ever had pituitary problems before
- · Anything else you have tried at home to manage the symptoms
- Note: Remind healthcare professionals outside the healthcare team that you are receiving immunotherapy for your cancer and it can affect your pituitary gland. This is particularly important if they are planning any scans of your head/brain

Red flag(s):

- For severe symptoms, call for an ambulance immediately and inform Acute Oncology service/on-call triage in the treating hospital
- For less severe symptoms, call Acute Oncology service/on-call triage in the treating hospital for instructions or go to the accident and emergency (A&E) department at the local hospital

Regardless of where you are being treated, be sure to inform the treating healthcare professional (HCP) that you are receiving immunotherapy and show them the documentation (eg, wallet card for your medication)

Taking care of your pituitary gland:

- · Eat a healthy diet and exercise regularly
- · Continue taking any thyroid supplements you were prescribed prior to starting cancer therapy



THYROID PROBLEMS OPDIVO[®] (nivolumab)

Report immediately to your consultant's office

What are the symptoms?

- Changes in your energy level (eg, more tired)
- Changes in your appetite (either you're more hungry or less hungry)
- If you have been losing or gaining weight without trying
- You are not able to tolerate hot or cold temperatures
- Changes in your mood, energy level, or behaviour such as decreased sex drive, irritability, or forgetfulness
- Your heart races, seems to skip a beat, or flutters
- You have constipation or diarrhoea
- Your skin is either drier or oilier than before
- Your hair is thinning

What you should tell your consultant:

- When you first noticed the symptoms above
- · How severe the symptoms are
- If the symptoms are interfering with your daily activities
- · A list of medications and supplements you're taking
- If you've ever had thyroid problems before
- Anything else you have tried at home to manage the symptoms

Red flag(s):

- For severe symptoms, call for an ambulance immediately and inform Acute Oncology service/on-call triage in the treating hospital
- For less severe symptoms, call Acute Oncology service/on-call triage in the treating hospital for instructions or go to the accident and emergency (A&E) department at the local hospital

Regardless of where you are being treated, be sure to inform the treating healthcare professional (HCP) that you are receiving immunotherapy and show them the documentation (eg, wallet card for your medication)

Taking care of your thyroid gland:

- Eat a healthy diet and exercise regularly
- . Continue taking any thyroid supplements you were prescribed prior to starting cancer therapy



DIABETES (HIGH BLOOD GLUCOSE, HYPERGLYCEMIA) OPDIVO® (nivolumab)

Report immediately to your consultant's office

What are the symptoms?

- More frequent urination
- You feel very tired

- Greater thirst
- Increased hunger

• Your breath smells sweet or fruity

What you should tell your consultant:

- When you first noticed the symptoms above
- · How severe the symptoms are
- If the symptoms are interfering with your daily activities
- · A list of medications and supplements you're taking
- If you've been told you have diabetes before
- · Anything else you have tried at home to manage the symptoms

Red flag(s):

- For severe symptoms, call for an ambulance immediately and inform Acute Oncology service/on-call triage in the treating hospital
- For less severe symptoms, call Acute Oncology service/on-call triage in the treating hospital for instructions or go to the accident and emergency (A&E) department at the local hospital

Regardless of where you are being treated, be sure to inform the treating healthcare professional (HCP) that you are receiving immunotherapy and show them the documentation (eg, wallet card for your medication)

Taking care of your pancreas:

Eat a healthy diet and exercise regularly



NERVE PROBLEMS OPDIVO[®] (nivolumab)

Report immediately to your consultant's office

What are the symptoms?

- Weakness on one or both sides of the body (legs, arms, or face)
- New or worsened pain, numbness, or tingling in the hands or feet
- Trouble walking

- Difficulty writing
- Tremors (shakes)
- Trouble holding items (dropping things)
- Having a hard time getting dressed (eg, buttoning buttons)

What you should tell your consultant:

- When you first noticed the symptoms above
- · How severe the symptoms are
- If the symptoms are interfering with your daily activities
- · A list of medications and supplements you're taking
- If you've ever had similar symptoms before, walking problems, or diabetes
- · Anything else you have tried at home to manage the symptoms

Red flag(s):

- For severe symptoms, call for an ambulance immediately and inform Acute Oncology service/on-call triage in the treating hospital
- For less severe symptoms, call Acute Oncology service/on-call triage in the treating hospital for instructions or go to the accident and emergency (A&E) department at the local hospital

Regardless of where you are being treated, be sure to inform the treating healthcare professional (HCP) that you are receiving immunotherapy and show them the documentation (eg, wallet card for your medication)



JOINT PAIN, SWELLING, OR STIFFNESS OPDIVO® (nivolumab)

Report immediately to your consultant's office

What are the symptoms?

- Joint pain
- Joint stiffness

• Difficulty with walking or performing your daily activities

- Joint swelling
- Redness around the joint

What you should tell your consultant:

- When these symptoms started, what brings them on, and how long they last
- · Which joints are affected
- If the symptoms are affecting your ability to do your daily activities
- If you have ever had any joint problems in the past and are those symptoms worsening
- If you also feel very tired
- If you have any associated skin changes
- · Anything else you have tried at home to manage the symptoms

Red flag(s):

- For severe symptoms, call for an ambulance immediately and inform Acute Oncology service/on-call triage in the treating hospital
- For less severe symptoms, call Acute Oncology service/on-call triage in the treating hospital for instructions or go to the accident and emergency (A&E) department at the local hospital

Regardless of where you are being treated, be sure to inform the treating healthcare professional (HCP) that you are receiving immunotherapy and show them the documentation (eg, wallet card for your medication)

Managing your side effects:

- With the approval of your consultant's office, take over-the-counter anti-inflammatories/pain relievers such as ibuprofen to relieve pain and stiffness. Your consultant may give you stronger prescription drugs to ease joint problems
- Apply an ice pack to swollen joints for 15 minutes several times a day
- · Keep the joint above your heart whenever you can to reduce swelling
- · Use elastic wrap or KT tape on the joint to support it
- Try to stay as active as possible. Do 30 minutes of low-to-moderate-intensity physical activity most days of the week. Also try to do resistance training (calisthenics or with weights), yoga, tai chi, Qigong, Pilates, aquatic exercise, or a focused dance program
- Avoid activities that cause pain



MUSCLE PAIN OR STIFFNESS OPDIVO® (nivolumab)

Report immediately to your consultant's office

What are the symptoms?

• Muscle pain •

• Muscle stiffness • Easily tired from activity

What you should tell your consultant:

- . When the symptom started and how it developed (slowly vs suddenly)
- · Whether you did any activity that might have caused it
- Whether you have had an injury
- · Whether you have had any changes to your medications
- Which muscles are affected
- · If the symptoms are affecting your ability to perform your daily activities
- If you have had muscular problems previously and those existing symptoms are getting worse
- If, in addition to muscle symptoms, you also feel very tired or short of breath
- Anything else you have tried at home to manage the symptoms

Red flag(s):

- For severe symptoms, call for an ambulance immediately and inform Acute Oncology service/on-call triage in the treating hospital
- For less severe symptoms, call Acute Oncology service/on-call triage in the treating hospital for instructions or go to the accident and emergency (A&E) department at the local hospital

Regardless of where you are being treated, be sure to inform the treating healthcare professional (HCP) that you are receiving immunotherapy and show them the documentation (eg, wallet card for your medication)

Managing your side effects:

- With the approval of your consultant's office, take over-the-counter anti-inflammatories/pain relievers such as ibuprofen to relieve pain and stiffness. Your consultant may give you stronger prescription drugs to ease joint problems
- · Apply heat or take a warm bath to relax the muscle
- Avoid activities that cause pain but do try to stretch and keep active



ADRENAL GLAND PROBLEMS OPDIVO® (nivolumab)

Report immediately to your consultant's office

What are the symptoms?

- Fatigue/low energy
- Muscle weakness
- Muscle pain
- Feeling dizzy/ lightheaded
- Feeling confused/foggy
- Feeling faint or actually fainting
- Nausea/vomiting
- Darkening/bronzing of skin
- Craving salty foods/drinks
- Feeling irritable or depressed
- Loss of appetite
- Weight loss

What you should tell your consultant:

- When you first noticed the symptoms above and if they developed slowly vs suddenly
- How severe the symptoms are
- If the symptoms are interfering with your daily activities
- If you have recently been stressed or ill
- A list of medications and supplements you're taking (including any steroids and recent dose changes)
- If you've ever had adrenal problems before
- · Anything you have tried at home to manage the symptoms

Red flag(s):

- For severe symptoms, call for an ambulance immediately and inform Acute Oncology service/on-call triage in the treating hospital
- For less severe symptoms, call Acute Oncology service/on-call triage in the treating hospital for instructions or go to the accident and emergency (A&E) department at the local hospital

Regardless of where you are being treated, be sure to inform the treating healthcare professional (HCP) that you are receiving immunotherapy and show them the documentation (eg, wallet card for your medication)

Taking care of your adrenal gland:

 If you have been diagnosed with an adrenal insufficiency, your healthcare team will educate you about wearing a medical alert bracelet and being prepared with stress doses of corticosteroids for surgery, severe illness, injury, etc.



OTHER SYMPTOMS TO LOOK OUT FOR

Below are other symptoms that you can have when you take OPDIVO[®] (nivolumab). We are very concerned about symptoms we have marked with a check mark. Please call the office if you develop any of these symptoms, and consider going directly to Accident and Emergency at your local hospital (A&E) if you have any of the red-flag symptoms.

\checkmark	Symptoms	Red flags (Signs that something serious is going on that needs immediate attention)
	Appetite changes (not feeling hungry or wanting to eat)	 If you have no appetite plus you feel faint, pass out, and/or have trouble thinking (cloudy thinking, confusion)
	Chest pain	 Any chest pain should be evaluated immediately
	Fatigue (feeling weak or tired)	 If you faint or have shortness of breath or chest pain
	Fever	 If you have a fever over 40°C If you also have breathing problems
	Headaches	 If you have a very painful headache (the "worst headache of your life"), head pain that doesn't go away after a few hours, or head pain with fever, neck pain or stiffness, and/or rash If you have head pain and changes in vision
	Nausea	 If you have uncontrolled nausea and it is limiting your ability to eat or drink
	Shortness of breath (difficulty catching your breath or getting enough air in your lungs)	 If you have any trouble breathing or worsening of your existing symptoms If you have shortness of breath plus chest pain and/or fainting If you have shortness of breath and swelling of the legs or leg pain



OTHER SYMPTOMS TO LOOK OUT FOR

(Continued)

\checkmark	Symptoms	Red flags (Signs that something serious is going on that needs immediate attention)
	Sleep changes (difficulty falling or staying asleep)	 Fatigue that is affecting your ability to function
	Vision and eye changes (blurry vision, double vision, or other vision problems; eye pain or redness)	 Sudden and severe symptoms, such as sudden vision changes, eye pain, or redness
	Vomiting (throwing up)	 If you go more than 24 hours without being able to hold down foods or liquids, and/or you vomit blood, your vomit looks like coffee grounds, or you have severe stomach pain
	Weight loss	 If you have no appetite plus you feel faint, pass out, and/or have trouble thinking (cloudy thinking, confusion)
Weakness (general or in your muscles)	 If you also have headaches and dizziness If weakness is on the face or one side of your body plus you have numbness, slurred speech, confusion, drooping in the face 	
	 If weakness is all over the body and you feel very tired and even faint, have a fever, and your heart is racing 	



RESOURCES

www.kcuk.org.uk

www.cancerresearchuk.org www.macmillan.org.uk