

## Nivolumab and Ipilimumab (for kidney cancer using extended dosing of ipilimumab)

NB: This regimen uses different doses to the nivolumab/ipilimumab combination regimen used in the treatment of melanoma, mesothelioma or colorectal cancer  
Check that the correct dosing regimen is being used

### Indication

First line treatment of intermediate or poor risk advanced renal cell carcinoma (RCC), extended dosing of ipilimumab based on the PRISM trial design

### Regimen details

**Weeks 1, 13, 25 and 37:**

Drug	Fluid	Route	Time
Nivolumab 3mg/kg	50ml Sodium chloride 0.9%	IV	30 mins
Ipilimumab 1mg/kg	50ml Sodium chloride 0.9%	IV	30 mins

**Every 2 weeks in weeks 3-11:**

Drug	Route	Time
Nivolumab 600mg	SC	3-5 mins

**Every 4 weeks in weeks 17,21,29,33 and from week 41 onwards:**

Drug	Route	Time
Nivolumab 1200mg	SC	3-5 mins

This will be displayed as cycles in iQemo:

Week	Cycle	Treatment given	
1	1	Ipilimumab & nivolumab	Cycles given 2-weekly
3	2	Nivolumab 600mg	
5	3	Nivolumab 600mg	
7	4	Nivolumab 600mg	
9	5	Nivolumab 600mg	
11	6	Nivolumab 600mg	
13	7	Ipilimumab & nivolumab	Cycles given 4-weekly
17	8	Nivolumab 1200mg	
21	9	Nivolumab 1200mg	
25	10	Ipilimumab & nivolumab	
29	11	Nivolumab 1200mg	
33	12	Nivolumab 1200mg	
37	13	Ipilimumab & nivolumab	
41+	14+	Nivolumab 1200mg	

### Cycle frequency

As above

### Number of cycles

As above, continued until disease progression or toxicity

## Administration

### Intravenous

Administer the drug solution using a volumetric pump through an intravenous line containing a sterile non-pyrogenic, low protein binding in-line filter (pore size of 0.2 micrometer to 1.2 micrometer)

When administered in combination, nivolumab should be given first

Patients should be monitored for infusion related reactions

### Subcutaneous (Nivolumab)

SC Nivolumab should be administered subcutaneously over 3-5 minutes into the subcutaneous tissue of the abdomen or thigh. Alternate injection sites for successive injections. Do not inject into areas where the skin is tender, red, or bruised, or areas where there are scars or moles. If the administration of OPDIVO solution for injection is interrupted, it can be resumed at the same site, or at an alternate site.

Allow the solution to reach ambient temperature before administration.

## Pre-medication

Nil

## Emetogenicity

No routine antiemetics required

## Additional supportive medication

Nil

## Extravasation

Neutral

## Investigations – pre first cycle

Investigation	Validity period
FBC	14 days
U+E (including creatinine and bicarbonate)	14 days
LFT (including AST)	14 days
Calcium	14 days
Serum samples for HIV, Hep C antibody and HBs Ag if risk factors	Baseline
Cortisol	Baseline
Luteinizing hormone	Baseline
Follicle stimulating hormone	Baseline
Testosterone	Baseline

## Cautions

Presence of HIV, hepatitis B or C

Patients on high dose immunosuppression

Autoimmune disease: history of active inflammatory bowel disease, history of symptomatic autoimmune disease e.g. rheumatoid arthritis, SLE, autoimmune vasculitis, history of autoimmune neuropathy e.g. Guillain-Barre

Patients should be on the lowest clinically effective dose of systemic steroids

No dose adjustment is required for mild-moderate renal impairment. No data are available for severe renal impairment (GFR <30ml/min)

No data are available for liver impairment (bilirubin >1.5 ULN)

## Investigations –pre subsequent cycles

FBC, U+E (including creatinine), LFT (including AST), TFTs every cycle for the first 4 doses, then routinely every other cycle or as per clinician instructions

## Standard limits for administration to go ahead

If blood results not within range, authorisation to administer **must** be given by prescriber/ consultant.

Investigation	Limit
Neutrophil count	$\geq 1.0 \times 10^9/L$
Platelet count	$\geq 75 \times 10^9/L$
Creatinine clearance	$\geq 30 \text{ mL/min}$
Bilirubin	$\leq 1.5 \times \text{ULN}$
AST	$< 2.5 \times \text{ULN}$ if no liver mets, $< 5 \times \text{ULN}$ if liver mets

## Dose modifications

Dose de-escalation and/or escalation of nivolumab or ipilimumab is otherwise not allowed.  
For information on treatment of Immune related side effects see:

<https://www.healthierlsc.co.uk/canceralliance/chemotherapy-protocols/immunotherapy-toxicity-guidelines>

## Adverse effects –

for full details consult product literature/ reference texts

### • Serious side effects

Immune reactions may occur during or after completion of treatment.

Infusion related reactions

Colitis

Hepatitis

Peripheral neuropathy

Hypopituitarism

Hypothyroidism

Uveitis

Renal failure

Cardiac events

Thromboembolism

Interstitial lung disease

Pneumonia, upper respiratory tract infection

### • Frequently occurring side effects

Pruritus

Rash

Nausea and vomiting

Diarrhoea

Fatigue

Decreased appetite

Abdominal pain

Hypertension

Arthralgia

### • Other side effects

Tumour pain

Headache, dizziness

Blurred vision

Raised transaminases

## Significant drug interactions

– for full details consult product literature/ reference texts

Anticoagulants: increased risk of haemorrhage – avoid or closely monitor.

Corticosteroids: use of systemic corticosteroids at baseline, before starting ipilimumab and/or nivolumab, should be avoided because of their potential interference with the pharmacodynamic activity and efficacy of the agents. However, systemic corticosteroids or other immunosuppressants can be used after starting ipilimumab and/or nivolumab to treat immune-related adverse reactions.

### Additional comments

Ipilimumab is contraindicated in patients with active, life-threatening autoimmune disease, or patients who are receiving immunosuppressive treatment following organ transplantation graft where immune activation is potentially imminently life threatening.

The prescriber must discuss the risks of nivolumab therapy with the patient and provide the Patient Alert Card.

Contraception: Adequate methods of contraception should be used during therapy and for 8 weeks after last dose.

Sodium: Ipilimumab and nivolumab concentrate each contain 0.1mmol (2.30mg) sodium per mL. Care if low sodium diet.

### References

Yervoy SPC - <https://www.medicines.org.uk/emc/product/4683>

Opdivo SPC - <https://www.medicines.org.uk/emc/product/6888>

OPDIVO 600 mg/5 ml solution for injection - Summary of Product Characteristics (SmPC) - (emc) | 100807

South West Clinical Network SACT protocols - <http://www.swscn.org.uk/guidance-protocols/cancer-protocols/>

Clatterbridge SACT protocol - [Nivolumab in combination with Ipilimumab Advanced Renal Cell Carcinoma](#)

Standard Versus Modified Ipilimumab, in Combination With Nivolumab, in Advanced Renal Cell Carcinoma: A Randomized Phase II Trial (PRISM) Naveen S. Vasudev et al Journal of Clinical Oncology 2024 42:3, 312-323

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**THIS PROTOCOL HAS BEEN DIRECTED BY DR PARIKH, DESIGNATED LEAD CLINICIAN FOR KIDNEY CANCER**

**RESPONSIBILITY FOR THIS PROTOCOL LIES WITH THE HEAD OF SERVICE**

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