

# Clinical Trials Landscape in Canada

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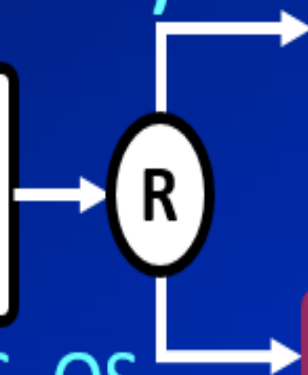
# First-Line Advanced or Metastatic Disease



# Phase III trials investigating PD-L1/PD-1 inhibitors plus VEGF inhibitors in 1L mRCC

## Checkmate 9ER (NCT03141177)

- Locally advanced or metastatic RCC with clear cell component  
N=630



Nivolumab + cabozantinib

Sunitinib

Co-primary endpoints: PFS, OS

Third arm Cabozantinib/Nivolumab/Ipilimumab arm discontinued

Recruitment ongoing

Results of Phase Ib recently reported

# Phase III trials investigating PD-L1/PD-1 inhibitors plus VEGF inhibitors in 1L mRCC

## CLEAR Study (NCT02811861)

- Locally advanced or metastatic RCC with clear cell component  
N=735

Co-primary endpoints: PFS, OS

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graph LR; A[Locally advanced or metastatic RCC with clear cell component N=735] --> B((R)); B --> C[Pembrolizumab + lenvatinib]; B --> D[Everolimus + lenvatinib]; B --> E[Sunitinib];
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Pembrolizumab +  
lenvatinib

Everolimus +  
lenvatinib

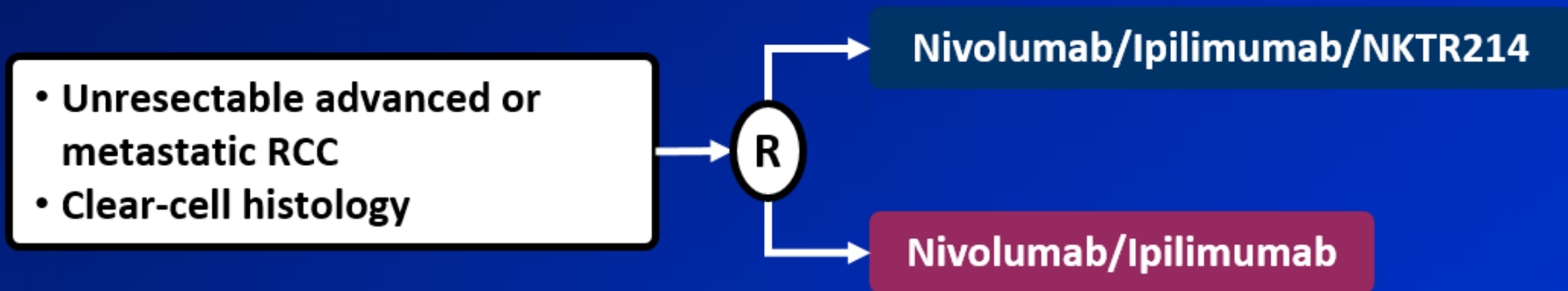
Sunitinib

Recruitment ongoing

Results of Phase Ib recently reported

# A Phase 3 Study Comparing NKTR-214 Combined with Nivolumab and Ipilimumab to Nivolumab and Ipilimumab Alone in Participants with Previously Untreated Intermediate- and Poor-Risk Advanced Renal Cell Carcinoma

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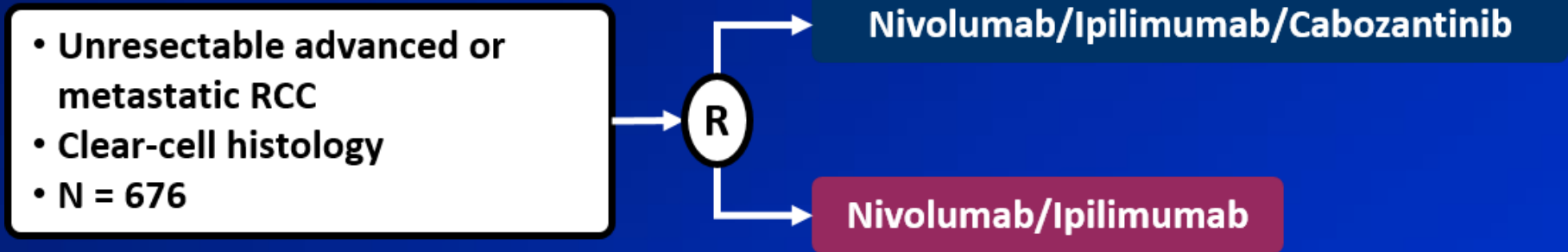


Co-primary endpoints: ORR, PFS, OS

- NKTR-214 = Bempegaldesleukin
- CD122-biased agonist
- CD122 = Interleukin-2 receptor beta subunit, is a key signaling receptor that is known to increase proliferation of these effector T cells.

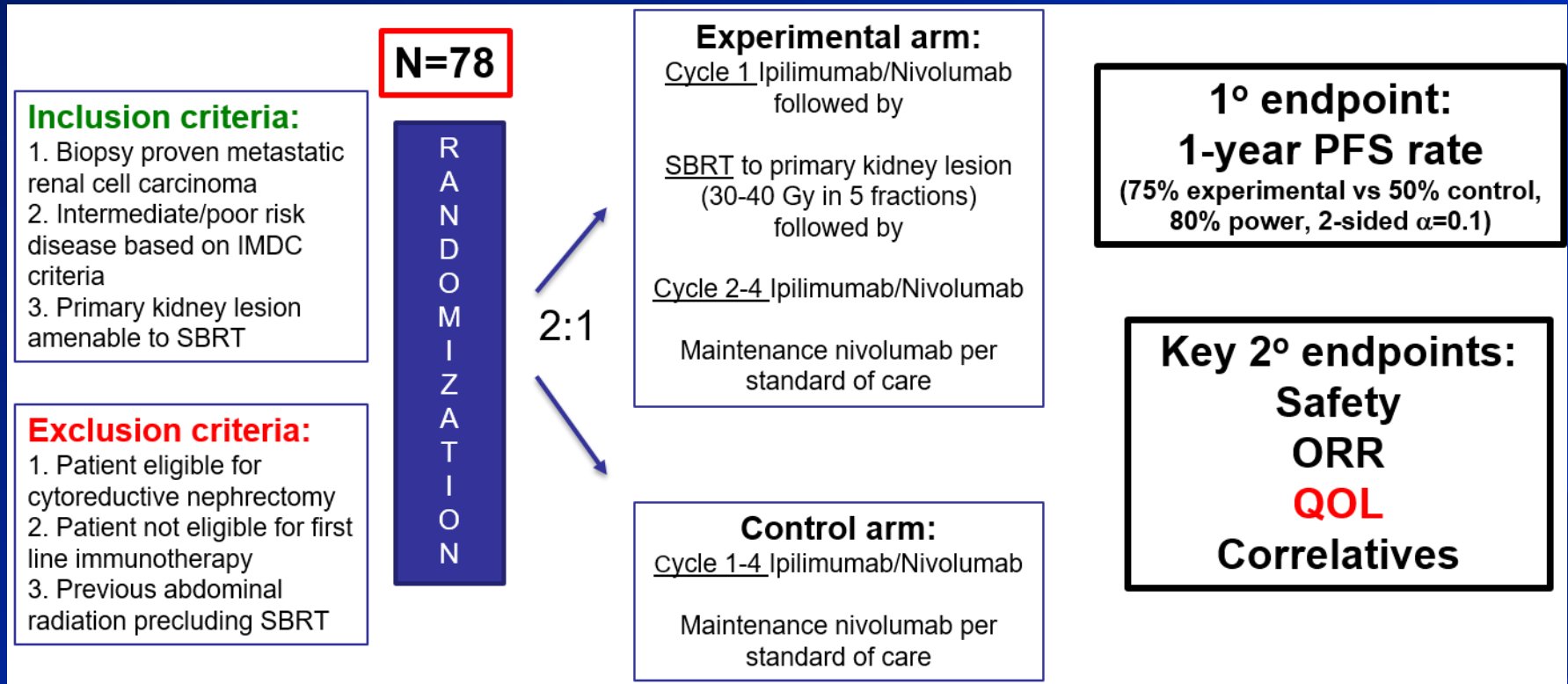
# A Randomized, Double-Blind, Controlled Phase 3 Study of Cabozantinib in Combination with Nivolumab and Ipilimumab versus Nivolumab and Ipilimumab in Previously Untreated Advanced or Metastatic Renal Cell Carcinoma of Intermediate or Poor Risk

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Primary endpoints: Duration of PFS

# Cytoreductive Stereotactic Hypofractionated Radiotherapy With Combination Ipilimumab/Nivolumab for Metastatic Kidney Cancer (CYTOSHRINK)



# Cytoreductive Stereotactic Hypofractionated Radiotherapy With Combination Ipilimumab/Nivolumab for Metastatic Kidney Cancer (CYTOSHRINK)

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Primary endpoints: 1 year PFS

2:1 randomization

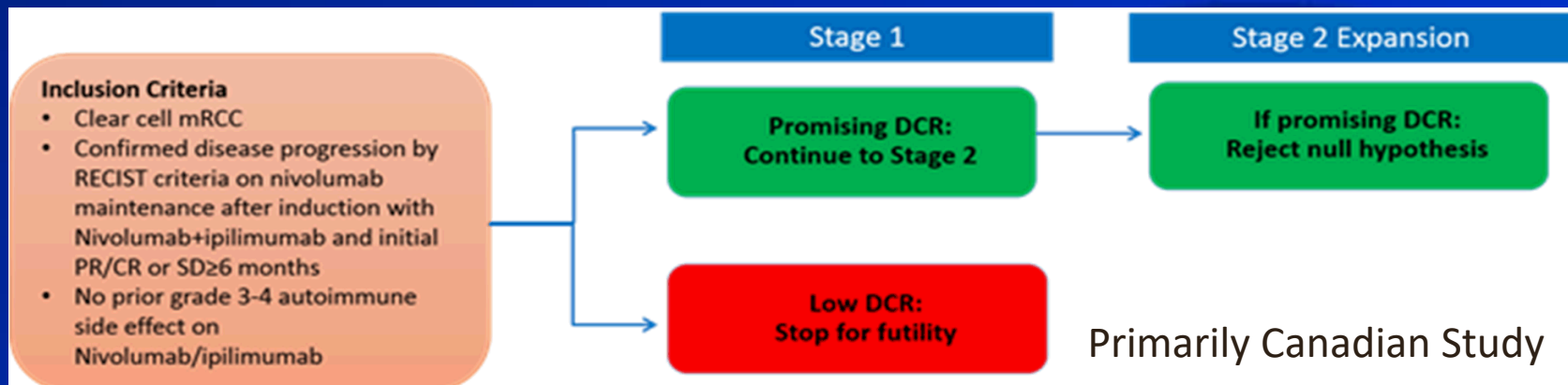
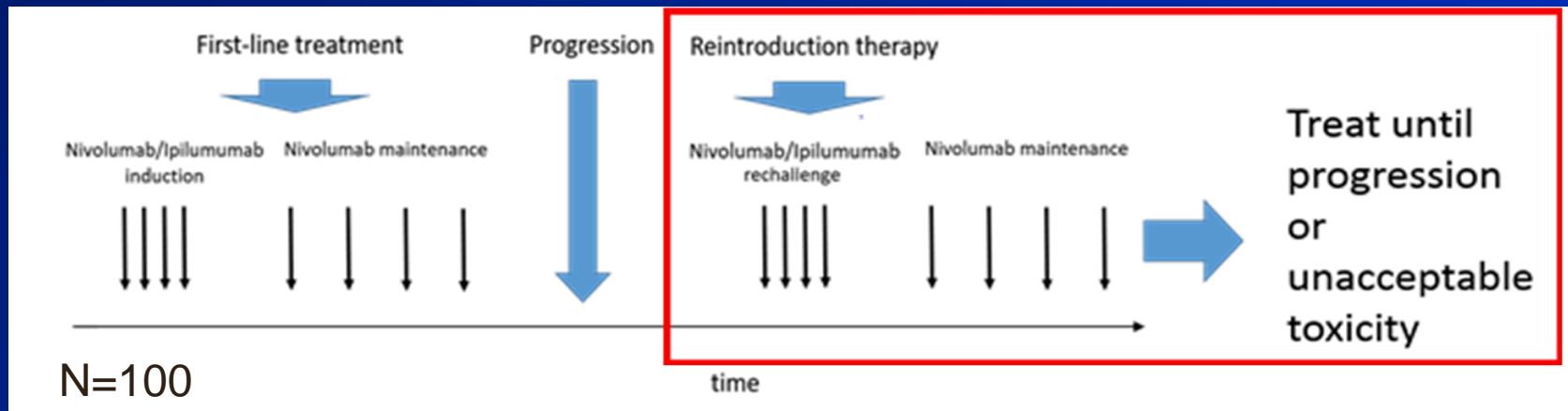
N = 78

- **Circulating blood markers:**
  - Baseline IL-6 and other cytokines/angiokines
  - Germline DNA and ctDNA
  - PBMCs
- **Quality of life: FKSI-19, PROMIS-Fatigue, and EQ5D-5L surveys**
- **Stool Microbiome (16S RNA, metagenomics)**

**Study Co-Chairs: A. Swaminath, A. Lalani, S. Hotte**  
Ontario study with Hamilton, London, Sunnybrook and Ottawa.



# A Phase 2, Single-arm Study of Combination Ipilimumab and Nivolumab Rechallenge in Renal Cell Carcinoma Patients Progressing on Nivolumab Maintenance Therapy After Ipilimumab and Nivolumab Induction



# Second Line and Beyond



# A Study to Test Combination (Immuno-oncology Drug) Treatments in Patients With Advanced Kidney Cancer: FRACTION RCC

## Randomized phase II: FRACTION-RCC

- Metastatic RCC
- Primary endpoint: PFS, ORR, DOR
- Secondary endpoint: Safety, Tolerability
- N = 200
- prior therapy permitted

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Nivolumab / Ipilimumab

Nivolumab + Relatlimab

(LAG-3 inhibitor)

Nivolumab + BMS-986205

(IDO-1 inhibitor)

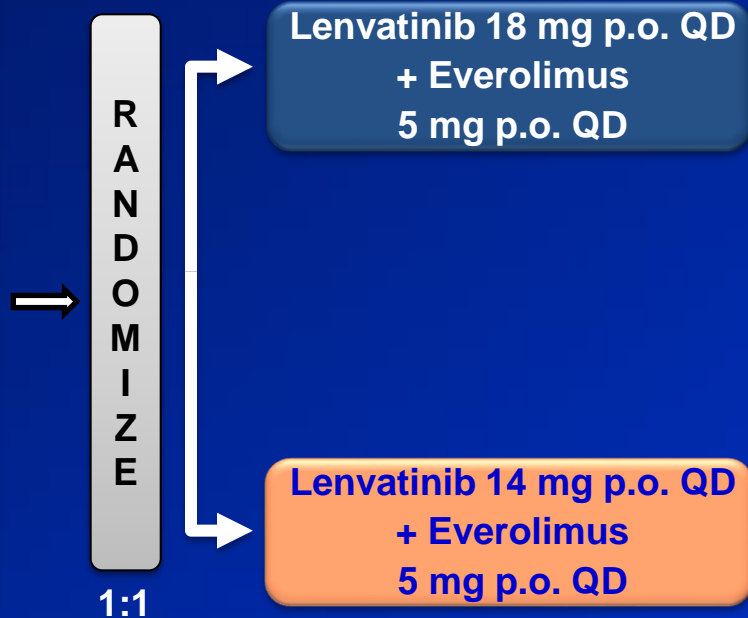
Recruitment ongoing

# Current Second/Third line Studies:

(N=306 subjects)

## Key eligibility criteria:

- Advanced RCC with a clear-cell component
- Measurable disease
- One prior disease progression episode on or after VEGF-targeted treatment
- **Prior PD-1/PD-L1 treatment in addition to 1 prior VEGF-targeted treatment**
- Karnofsky Performance Status  $\geq$  70



**Primary endpoint:**  
ORR (week 24), Safety (week 24)

**Secondary endpoints:**  
ORR, PFS, OS, Safety, HRQOL, PFS2, PK/PD

## Stratification by:

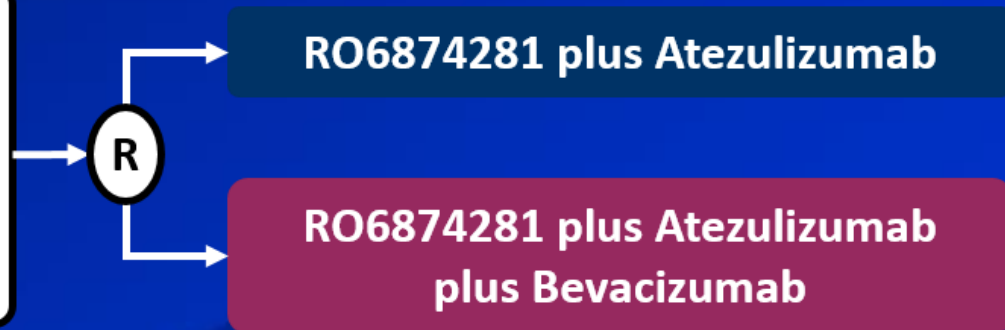
- **MSKCC prognostic groups** (favorable, intermediate and poor risk)
- **Prior PD-1/PD-L1 treatment** (yes and no)

Recruitment ongoing

# Study to Evaluate Safety, Pharmacokinetics and Therapeutic Activity of RO6874281 as a Combination Therapy in Participants With Unresectable Advanced and/or Metastatic Renal Cell Carcinoma (RCC)

Randomized phase II: RO6874281 (anti-FAP/interleukin-2 fusion protein RO6874281)

- Metastatic RCC
- Clear-cell histology
- Primary endpoint: DLT, MTD, ORR
- N = 190
- One prior VEGFR inhibitor permitted

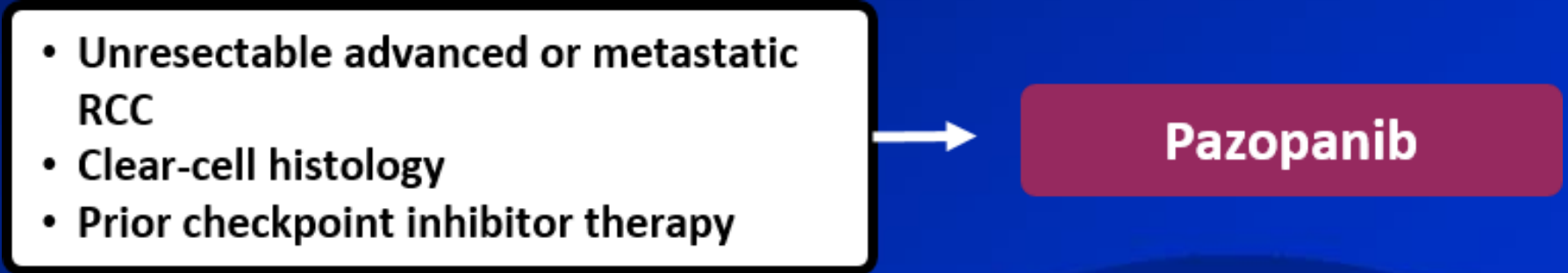


Recruitment ongoing

# Study of Efficacy, Safety, and Quality of Life of Pazopanib in Patients With Advanced and/or Metastatic Renal Cell Carcinoma After Prior Checkpoint Inhibitor Treatment (IO-PAZ)

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Phase II: n = 100 with 1 or 2 prior lines of therapy

- Unresectable advanced or metastatic RCC
  - Clear-cell histology
  - Prior checkpoint inhibitor therapy
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graph LR; A["• Unresectable advanced or metastatic RCC  
• Clear-cell histology  
• Prior checkpoint inhibitor therapy"] --> B[Pazopanib]
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**Pazopanib**

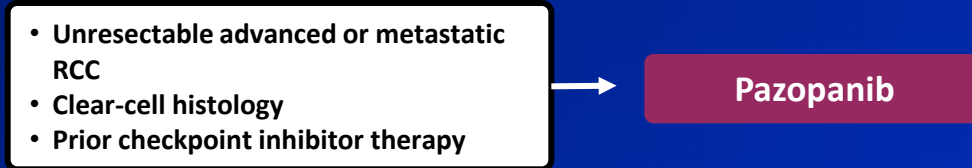
Primary endpoints: PFS

Recruitment ongoing

# Study of Efficacy, Safety, and Quality of Life of Pazopanib in Patients With Advanced and/or Metastatic Renal Cell Carcinoma After Prior Checkpoint Inhibitor Treatment (IO-PAZ)

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Phase II: n = 100 with 1 or 2 prior lines of therapy



Primary endpoints: PFS

Recruitment ongoing

# Adjuvant Studies



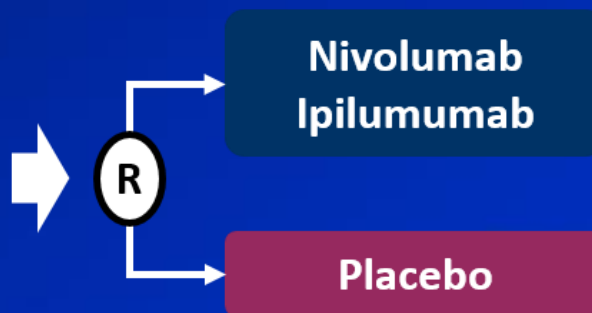


# Adjuvant Studies:

## A Study Comparing the Combination of Nivolumab and Ipilimumab Versus Placebo in Patients With Localized Kidney Cancer

Randomized phase III: Checkmate 914

- Localized RCC
- Clear-cell histology
- Primary endpoint: DFS
- Secondary endpoint: OS
- pT2a, G3 or G4, N0 M0; pT2b, G any, N0 M0; pT3, G any, N0 M0; pT4, G any, N0 M0; pT any, G any, N1 M0



N = 800

Recruitment ongoing

# Adjuvant Studies:

## A Study of Atezolizumab as Adjuvant Therapy in Patients with Kidney Cancer at High Risk of Developing Metastasis After a Nephrectomy

Randomized phase III: IMmotion 010

- Localized RCC
- Clear-cell histology
- N = 664
- Primary endpoint: DFS
- Secondary endpoint: OS
- T2 Grade 4, T3a Grade 3-4, T3b/c any Grade, T4 any Grade or TxN+ any Grade
- have had complete resection of limited metachronous/synchronous metastasis



Recruitment ongoing

# Adjuvant Studies: A Study of Pembrolizumab as Adjuvant Therapy in Patients After a Nephrectomy

Randomized phase III: Keynote 564

- Localized RCC
- Clear-cell histology
- N = 950
- Primary endpoint: DFS
- Secondary endpoint: OS
- Intermediate risk: pT2, Grade 4 or sarcomatoid, N0, M0; pT3, Any Grade, N0, M0
- High risk RCC: pT4, Any Grade N0, M0; pT, Any stage, Any Grade, N+, M0
- have had complete resection of limited metachronous/synchronous metastasis

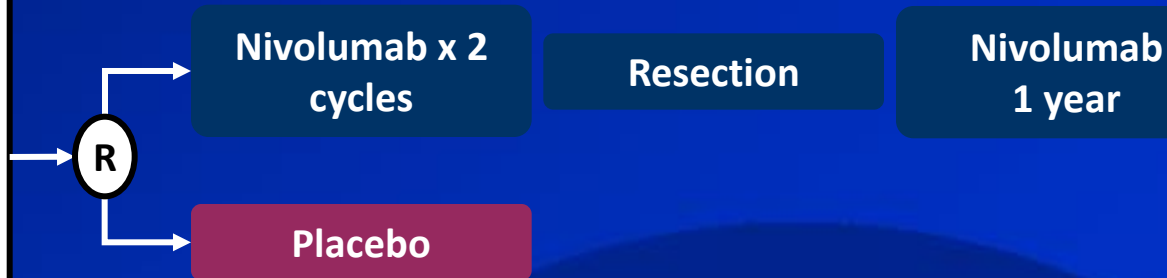


Recruitment ongoing

# Adjuvant Studies: Nivolumab in Treating Patients With Localized Kidney Cancer Undergoing Surgery with a Nephrectomy

Randomized phase III: **PROSPER**

- Localized RCC
- Clear-cell histology
- Primary endpoint: RFS
- Secondary endpoint: OS
- N = 766
- Clinical stage  $\geq$  T2NxM0 or TanyN+ disease



Recruitment ongoing

# Phase I Studies




# Phase I Studies

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- Increasing number of phase I studies examining various immunotherapy combinations
- Immunotherapy naïve and immunotherapy pretreated patients
  - BMS-986178 (anti-OX40) by Itself or in Combination With Nivolumab, in Combination with Ipilimumab, or a Combination of all 3 Drugs
  - Anti-LAG-3 (Relatlimab) With and Without an Anti-PD-1 (Nivolumab)
  - LAG525 (anti Lag3) ± spartalizumab (PD1 inhibitor)
  - CPI-444 (adenosine receptor inhibitor) Given by Itself and also in Combination With Atezolizumab
  - Pembrolizumab and Ziv-aflibercept
  - NKTR-214 in Combination with Nivolumab or in Combination with Nivolumab and Ipilimumab

# Conclusions:

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- Canadian Centers contribute significantly to a wide range of RCC studies
  - Increasing numbers of studies are opened
  - Increasing number of patients are recruited to clinical trials
  - Clinical trials are an important mean to offer novel and additional therapies to our patients
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# Studies involving Radiation



# A Phase II, Multi-Centre Study, of Stereotactic Radiotherapy for Oligo-Progression in Metastatic Renal Cell Cancer Patients Receiving 1st Line Sunitinib Therapy (OZM-053)

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- Stereotactic radiotherapy will be administered for up to five areas of metastatic sites showing oligo-progression within the same time period.
- N = 68
- Primary endpoint: To evaluate local control at one year of metastases treated with stereotactic radiotherapy in patients who present with oligo-progression while receiving first-line treatment with Sunitinib.

# A Phase II Proof of Principle Study of the Activity of Pembrolizumab (MK-3475) in Combination With SBRT in Primary Tyrosine Kinase Inhibitor (TKI) Refractory Metastatic Kidney Cancer (mRCC) Patients (OZM-065)

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Patients with progressive Disease as best response to first-line TKI

Arm A: Pembrolizumab will be started and Stereotactic Body Radiation Therapy will be given at the time of progression on pembrolizumab and pembrolizumab will be continued.

Arm B: Pembrolizumab will be started. Stereotactic Body Radiation Therapy will be given before the 2nd course of pembrolizumab and pembrolizumab will be continued.

N = 35

Primary Endpoint: Progression-free survival, as per ir-RECIST

## Other Radiation Studies:

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A Phase II, Multi-centre Study, of Combining Radiosurgery and Nivolumab in the Treatment of Brain Metastases From Non-small Cell Lung Cancer and Renal Cell Cancer (CHUM)

A Phase II Study on the Toxicity and Efficacy of a Normal Tissue Tolerance Adapted, 5 Fraction Stereotactic Body Radiation Therapy (SBRT) Regimen, for Extra-Cranial Oligometastases (UHN)

A Phase I Study Evaluating the Integration of Hypofractionated Renal Ablative Radiotherapy in the Setting of Metastatic Renal Cell Carcinoma (Lawson Health Center, London Ontario)



all studies recruiting