Open clinical uro-oncology trials in Canada

George Rodrigues, MD, Eric Winquist, MD
London Health Sciences Centre, London, Ontario, Canada

BLADDER CANCER

A PHASE II PROTOCOL FOR PATIENTS WITH STAGE T1 BLADDER CANCER TO EVALUATE SELECTIVE BLADDER PRESERVING TREATMENT BY RADIATION THERAPY CONCURRENT WITH CISPLATIN CHEMOTHERAPY FOLLOWING A THOROUGH TRANSURETHRAL SURGICAL RE-STAGING

Trial ID: RTOG 0926
Coordination: Radiation Therapy Oncology Group (RTOG)
Trial design: A randomized phase II study assessing a bladder preservation strategy for T1G2G3 bladder cancer.
Patient population: Operable patients with stage T1 disease (T1G2 or T1G3) for whom radical cystectomy is being considered as the next conventional step in therapy by standard urologic guidelines.
Sample size & primary endpoint: n = 37, rate of freedom from radical cystectomy at 3 years

PROSTATE ADENOCARCINOMA

LOCALIZED PROSTATE CANCER

Low Risk

A RANDOMIZED PHASE II TRIAL OF HYPOFRACTIONATED RADIOTHERAPY FOR FAVORABLE RISK PROSTATE CANCER

Trial ID: RTOG 0938
Coordination: Radiation Therapy Oncology Group (RTOG)
Trial design: A randomized phase II study assessing two hypo fractionated radiotherapy regimens in low risk prostate cancer.
Patient population: Histologically confirmed diagnosis of adenocarcinoma of the prostate within 180 days of randomization; Gleason scores 2-6; Clinical stage T1-2a; PSA < 10 ng/mL.
Sample size & primary endpoint: n = 174, EPIC Bowel score at 1 year after therapy

Intermediate Risk

A PHASE III PROSPECTIVE RANDOMIZED TRIAL OF DOSE-ESCALATED RADIOTHERAPY WITH OR WITHOUT SHORT TERM ANDROGEN DEPRIVATION THERAPY FOR PATIENTS WITH INTERMEDIATE RISK PROSTATE CANCER

Trial ID: RTOG 0815
Coordination: RTOG
Trial design: A randomized controlled trial to demonstrate an overall survival (OS) advantage for the addition of short term (6 months) ADT versus no additional ADT in the context of dose escalated RT for patients with intermediate risk prostate cancer.
Sample size & primary endpoint: n = 1520, overall survival

PROSTATE FRACTIONATED IRRADIATION TRIAL (PROFIT)

Coordination: Ontario Clinical Oncology Group (OCOG)

Trial design: A phase III study assessing the relative efficacy of dose-escalated radiation therapy (78 Gy in 39 fractions) versus a hypofractionated course of radiation (6000 Gy in 20 fractions).

Patient population: Intermediate-risk prostate cancer.

Sample size & primary endpoint: n = 1204, biochemical (PSA) failure

A RANDOMIZED, DOUBLE-BLINDED, PLACEBO-CONTROLLED PHASE III TRIAL TO EVALUATE THE EFFECTIVENESS OF A PHOSPHODIESTERASE 5 INHIBITOR, TADALAFIL, IN PREVENTION OF ERECTILE DYSFUNCTION IN PATIENTS TREATED WITH RADIOTHERAPY FOR PROSTATE CANCER

Trial ID: RTOG 0831

Coordination: RTOG

Trial design: A phase III placebo randomized trial to determine whether tadalafil maintains spontaneous (off-drug) erectile function, as measured by the International Index of Erectile Function (IIEF), as compared to placebo at weeks 28-30 after initiation of radiation therapy for prostate cancer.

Patient population: Men with clinical stage T1b-T2b adenocarcinoma of the prostate and no distant metastases (M0), and their spouses/partners.

Sample size & primary endpoint: n = 218, International Index of Erectile Function Questionnaire (IIEF)

High Risk

ANDROGEN DEPRIVATION THERAPY AND HIGH DOSE RADIOTHERAPY WITH OR WITHOUT WHOLE-PELVIC RADIOTHERAPY IN UNFAVORABLE INTERMEDIATE OR FAVORABLE HIGH RISK PROSTATE CANCER: A PHASE III RANDOMIZED TRIAL

Trial ID: RTOG 0924

Coordination: RTOG

Trial design: Demonstrate that prophylactic neoadjuvant androgen deprivation therapy (NADT) and whole-pelvic radiation therapy (WPRT) will result in improvement in overall survival (OS) in patients with "unfavorable" intermediate risk or "favorable" high risk prostate cancer compared to NADT and high dose prostate and seminal vesicle (SV) radiation therapy (P + SV RT) using intensity modulated radiotherapy (IMRT) or EBRT with a high dose rate (HDR) or a permanent prostate (radioactive seed) implant (PPI) boost in a phase III clinical trial.

Patient population: Patients who are most likely to benefit from androgen deprivation therapy and whole-pelvic radiotherapy, defined as: a) Having a significant risk of lymph node involvement (e.g. > 15%, based on the Roach formula) OR b) Being in one of the following risk groups: GS 7-10 + T1c-T2b (palpation) + PSA < 50 ng/mL (includes intermediate and high risk patients) GS 6 + T2c-T4 (palpation) or > 50% biopsies + PSA < 50 ng/mL GS 6 + T1c-T2b (palpation) + PSA > 20 ng/mL.

Sample size & primary endpoint: n = 2580 for a primary endpoint of overall survival

RANDOMIZED PHASE III STUDY OF NEO-ADJUVANT DOCETAXEL AND ANDROGEN DEPRIVATION PRIOR TO RADICAL PROSTATECTOMY VERSUS IMMEDIATE RADICAL PROSTATECTOMY IN PATIENTS WITH HIGH-RISK, CLINICALLY LOCALIZED PROSTATE CANCER

Trial ID: NCIC PRC3
Coordination: Intergroup (Cancer and Leukemia Group B)
Trial design: A phase III comparison of neoadjuvant chemohormonal therapy with goserelin or leuprolide for 18-24 weeks with docetaxel IV every 3 weeks for up to six courses followed by radical prostatectomy with staging pelvic lymphadenectomy versus radical prostatectomy with staging lymphadenectomy alone.
Patient population: High-risk prostate cancer.
Sample size & primary endpoint: n = 750, 3 year biochemical progression-free survival

POST-RADICAL PROSTATECTOMY

RADICALS: RADIOTHERAPY AND ANDROGEN DEPRIVATION IN COMBINATION AFTER LOCAL SURGERY

Trial ID: NCIC PR13
Coordination: Intergroup (MRC)
Trial design: Phase III clinical trial with randomizations both for radiotherapy timing, and for hormone treatment duration.
Patient population: Men who have undergone radical prostatectomy for prostatic adenocarcinoma within 3 months, post-operative serum PSA less than 0.4 ng/ml. Uncertainty in the opinion of the physician and patient regarding the need for immediate post-operative RT.
Sample size & primary endpoint: n = 5100, disease free survival

BIOCHEMICALLY RELAPSED PROSTATE CANCER

A MULTICENTER CLINICAL STUDY OF THE SONABLATE® 500 (SB-500) FOR THE TREATMENT OF LOCALLY RECURRENT PROSTATE CANCER WITH HIFU

Trial ID: FSI-003
Coordination: Focus Surgery Inc.
Trial design: Single arm phase II.
Patient population: Men with locally recurrent prostate cancer following external beam irradiation.
Sample size & primary endpoint: n = 202, absence of biochemical failure and negative prostate biopsy rate at 12 months

A PROSPECTIVE PHASE II TRIAL OF TRANSPERINEAL ULTRASOUND-GUIDED BRACHYTHERAPY FOR LOCALLY RECURRENT PROSTATE ADENOCARCINOMA FOLLOWING EXTERNAL BEAM RADIOTHERAPY

Trial ID: RTOG 0526
Coordination: RTOG
Trial design: Single arm phase II.
Patient population: Men with biopsy-documented local recurrence > 30 months after external beam radiotherapy.
Sample size & primary endpoint: n = 96, late treatment-related GI/GU adverse events of brachytherapy

A PHASE II TRIAL OF SHORT-TERM ANDROGEN DEPRIVATION WITH PELVIC LYMPH NODE OR PROSTATE BED ONLY RADIOTHERAPY (SPPORT) IN PROSTATE CANCER PATIENTS WITH A RISING PSA AFTER RADICAL PROSTATECTOMY

Trial ID: RTOG 0534
Coordination: RTOG
Trial design: Phase II comparing radiotherapy alone to radiotherapy with short-term androgen deprivation.
Patient population: Males who have undergone radical prostatectomy, followed by PSA rise to > 0.2 ng/ml.
Sample size & primary endpoint: n = 1764, 5-year freedom from progression

A STUDY OF ANDROGEN DEPRIVATION WITH LEUPROLIDE, +/- DOCETAXEL FOR CLINICALLY ASYMPTOMATIC PROSTATE CANCER SUBJECTS WITH A RISING PSA

Trial ID: XRP6976J/3503
Coordination: sanofi-aventis
Trial design: A phase III comparison of androgen deprivation with or without docetaxel in men with rising PSA followed by radical prostatectomy.
Patient population: No metastases and PSA doubling time $\leq$ 9 months
Sample size & primary endpoint: n = 412, progression-free survival

METASTATIC PROSTATE CANCER

A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED PHASE III STUDY OF EARLY VERSUS STANDARD ZOLEDRONIC ACID TO PREVENT SKELETAL RELATED EVENTS IN MEN WITH PROSTATE CANCER METASTATIC TO BONE

Trial ID: NCIC PRC2
Coordination: Intergroup (Cancer and Leukemia Group B)
Trial design: A phase III study comparing treatment with zoledronic acid at the time of initiation of androgen deprivation therapy for metastatic prostate cancer to treatment at time of progression to hormone-refractory disease.
Patient population: Metastatic prostate cancer with at least one bone metastasis by radiographic imaging receiving androgen deprivation therapy.
Sample size & primary endpoint: n = 680, time to first skeletal related event

CASTRATE RESISTANT PROSTATE CANCER

A MULTINATIONAL PHASE III, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED EFFICACY AND SAFETY STUDY OF ORAL MDV3100 IN CHEMOTHERAPY-NAÏVE PATIENTS WITH PROGRESSIVE METASTATIC PROSTATE CANCER WHO HAVE FAILED ANDROGEN DEPRIVATION THERAPY

Trial ID: PREVAIL
Coordination: Medivation/ProTrials Research Inc.
Trial design: Randomized double-blind multicentre study comparing MDV3100 to placebo.
Patient population: Asymptomatic metastatic castration-resistant prostate cancer and no prior chemotherapy.
Sample size & primary endpoint: n=1680, progression-free and overall survival

A PHASE III, RANDOMIZED, DOUBLE-BLIND, MULTICENTER TRIAL COMPARING ORTERONEL PLUS PREDNISONE WITH PLACEBO PLUS PREDNISONE IN PATIENTS WITH CHEMOTHERAPY-NAIVE METASTATIC CASTRATION-RESISTANT PROSTATE CANCER

Trial ID: NCT01193244
Coordination: Millennium Pharmaceuticals, Inc.
Trial design: Phase III.
Patient population: Asymptomatic metastatic castration-resistant prostate cancer and no prior chemotherapy.
Sample size & primary endpoint: n = 1454, radiographic progression-free survival and overall survival

A RANDOMIZED PHASE III STUDY COMPARING STANDARD FIRST-LINE DOCETAXEL/PREDNISONE TO DOCETAXEL/PREDNISONE IN COMBINATION WITH CUSTIRSEN (OGX-011) IN MEN WITH METASTATIC CASTRATE RESISTANT PROSTATE CANCER

Trial ID: SYNERGY
Coordination: Teva/Oncogenex
Trial design: Randomized multicentre study of the addition of custirsen to docetaxel chemotherapy.
Patient population: Metastatic castration-resistant prostate cancer planned for treatment with docetaxel.
Sample size & primary endpoint: n=800, overall survival

A RANDOMIZED, OPEN LABEL, MULTI-CENTER STUDY COMPARING CABAZITAXEL AT 25 MG/M2 AND AT 20 MG/M2 IN COMBINATION WITH PREDNISONE EVERY 3 WEEKS TO DOCETAXEL IN COMBINATION WITH PREDNISONE IN PATIENTS WITH METASTATIC CASTRATION RESISTANT PROSTATE CANCER NOT PRETREATED WITH CHEMOTHERAPY

Trial ID: NCT01308567
Coordination: sanofi aventis
Trial design: Phase III
Patient population: Metastatic castration resistant prostate cancer and not previously treated with chemotherapy.
Sample size & primary endpoint: n = 1170, overall survival

A PHASE II STUDY OF MAINTENANCE THERAPY WITH TEMSIROLIMUS IN ANDROGEN-INDEPENDENT PROSTATE CANCER AFTER FIRST LINE CHEMOTHERAPY WITH DOCETAXEL

Trial ID: OZM-018
Coordination: Sunnybrook Health Sciences Centre Odette Cancer Centre
Trial design: Single arm phase II.
Patient population: CRPC in remission after docetaxel.
Sample size & primary endpoint: n = 30, time to treatment failure

A MULTICENTRE, SINGLE-ARM, OPEN LABEL CLINICAL TRIAL INTENDED TO PROVIDE EARLY ACCESS TO CABAZITAXEL IN PATIENTS WITH METASTATIC HORMONE REFRACTORY PROSTATE CANCER PREVIOUSLY TREATED WITH A DOCETAXEL-CONTAINING REGIMEN AND TO DOCUMENT SAFETY OF CABAZITAXEL IN THESE PATIENTS

Trial ID: NCT01254279
Coordination: sanofi aventis
Trial design: Phase III.
Patient population: Metastatic hormone refractory prostate cancer previously treated with a docetaxel-containing regimen.
Sample size & primary endpoint: n = 808, overall survival

RANDOMIZED, OPEN LABEL MULTI-CENTER STUDY COMPARING CABAZITAXEL AT 20 MG/M2 AND AT 25 MG/M2 EVERY 3 WEEKS IN COMBINATION WITH PREDNISONE FOR THE TREATMENT OF METASTATIC CASTRATION RESISTANT PROSTATE CANCER PREVIOUSLY TREATED WITH A DOCETAXEL-CONTAINING REGIMEN

Trial ID: NCT01308580
Coordination: sanofi aventis
Trial design: Phase III.
Patient population: Metastatic castration resistant previously treated with a docetaxel-containing regimen.
Sample size & primary endpoint: n = 1200, overall survival

RENAL CELL CANCER

A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED PHASE THERAPY FOR SUBJECTS WITH LOCALIZED OR LOCALLY ADVANCED RCC FOLLOWING NEPHRECTOMY III STUDY TO EVALUATE THE EFFICACY AND SAFETY OF PAZOPANIB AS ADJUVANT

Trial ID: PROTECT/VEG113387
Coordination: GlaxoSmithKline Inc.
Trial design: Double-blind placebo-controlled phase III.
Patient population: Resected predominantly clear cell renal cell cancer at higher risk of recurrence.
Sample size & primary endpoint: n = 1500, disease-free survival

A RANDOMIZED PHASE II STUDY OF AFINITOR (RAD001) VS SUTENT (SUNITINIB) IN PATIENTS WITH METASTATIC NON-CLEAR CELL RENAL CELL CARCINOMA

Trial ID: ASPEN/NCT01108445
Coordination: Duke University
Trial design: Double-blind placebo-controlled phase III.
Patient population: Measurable metastatic predominantly non-clear cell renal cell cancer.
Sample size & primary endpoint: n = 108, progression-free survival

A PHASE II STUDY OF RO4929097 IN PATIENTS WITH ADVANCED RENAL CELL CARCINOMA THAT HAS PROGRESSED AFTER VEGF/VEGFR DIRECTED THERAPY

Trial ID: PHL-077
Coordination: Princess Margaret Hospital Phase II Consortium
Trial design: Single arm 2-stage phase II.
Patient population: Metastatic predominantly clear cell renal cell carcinoma with measurable disease treated with at least one prior antiangiogenic therapy (+/- one mTOR inhibitor).
Sample size & primary endpoint: n = 39, objective response rate

A RANDOMIZED, BLINDED, PHASE 2 DOSE-RANGING STUDY OF BMS-936558 (MDX-1106) IN SUBJECTS WITH PROGRESSIVE ADVANCED/METASTATIC CLEAR-CELL RENAL CELL CARCINOMA WHO HAVE RECEIVED PRIOR ANTI-ANGIOGENIC THERAPY

Trial ID: NCT01354431
Coordination: Bristol-Myers Squibb
Trial design: Phase II.
Patient population: Patients with either progressive and/or advanced/metastatic Clear-Cell Renal Cell Carcinoma after prior antiangiogenic treatment.
Sample size & primary endpoint: n = 39, objective response rate