A Phase I/II trial of BNC105P with everolimus in metastatic renal cell carcinoma (mRCC) patients: Updated Phase I results of the DisrupTOR-1 trial (Hoosier Oncology Group)

**Background**

-  **Everolimus**: Orally administered (10 mg) daily; 7 day lead in prior to administration of BNC105P.
-  **BNC105P**: Administered by IV injection over 10 minutes on Day 1 & Day 8 every 21 days.

**Methods**

- **Study Objectives**
  - To determine the dose limiting toxicities (DLTs) and no evidence of cumulative toxicities following treatment duration of up to 18 months.
  - To evaluate the adverse events of the combination.
  - To determine response rate and overall survival (max. 5 years) with combination therapy compared to everolimus alone.

**Key Eligibility Criteria**

- ** Eligibility:** Patients with newly diagnosed mRCC (clear cell, papillary, chromophobe).
- ** Inclusion:**
  - Karnofsky Performance Status (KPS) ≥ 70.
  - Life expectancy ≥ 6 months.
  - No evidence of active brain metastases.
  - No prior treatment with temsirolimus or everolimus in the Phase II component.
- ** Exclusion:**
  - Measurable disease according to RECIST.
  - Prolonged coagulopathy.
  - Uncontrolled hypertension.

**Phase II Dosing & Safety Data**

-  **Phase I**:
  - 4 dose levels of BNC105P, 3+3 design, N=12
  - No DLTs and no evidence of cumulative toxicities following treatment duration of up to 18 months.

-  **Phase II**:
  - 16 mg/m² Everolimus: orally administered (10 mg) daily; 7 day lead in prior to administration of BNC105P.
  - 10 mg oral, daily for 24 weeks

**Phase I/II Results**

- **Key biomarker in Phase I patients (N=12):**
  - Decreased expression of CDX2 and E-cadherin.
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**Phase I Biomarker Analysis**

- **Pathway:**
  - Wnt/β-catenin
  - EMT

**Conclusions**

- The combination in the Phase I patients indicates no drug-drug interactions between BNC105P and everolimus.
- The combination of everolimus and BNC105P is well tolerated with no dose limiting toxicities in the Phase I part of the study.
- The combination in the Phase I patients achieved disease stabilization.
- The combination of everolimus and BNC105P is well tolerated with no dose limiting toxicities in the Phase I part of the study.
- Decreases in biomarkers associated with vascular response suggest that BNC105P reaches greater levels of pharmacological significance. Changes in biomarkers will be compared with those in the Phase I trial.