Phase III study of a BNC105/p everolimus regimen for progressive renal cell carcinoma (mTORC1 inhibitor) (Hoosier Oncology Group)

Methods

Protocol #: GU09-145

Background

Everolimus: 10 mg oral, daily
BNC105P: 4.2 mg/m²
Everolimus: 10 mg oral, daily
BNC105P: 8.4 mg/m²
Everolimus: 10 mg oral, daily
BNC105P: 16 mg/m²
Everolimus: 10 mg oral, daily

Objectives

1. To determine PFS with BNC105P alone in patients progressing on everolimus.

2. To determine whether the combined use of this VDA with an agent active against mTOR may improve clinical outcome.

3. To determine if BNC105P is safe and well tolerated when combined with everolimus.

Study Design

- A 2-arm phase II randomized dose escalation study with 3 dose levels of BNC105P and 3 dose levels of everolimus, with 4 patients per dose level.

- The primary dose-finding endpoint is the occurrence of DLTs.

- Phase I dose escalation will be conducted in ascending order:
  - BNC105P: 4.2 mg/m², C1D1 (n=3)
  - BNC105P: 8.4 mg/m², C1D8 (n=4)
  - BNC105P: 12.6 mg/m², C1D1 (n=4)
  - BNC105P: 16 mg/m², C1D1 (n=3)

- Phase II dose escalation will be conducted in ascending order:
  - Everolimus: 10 mg oral, daily

- The phase III component of the study commenced in September 2011 and is ongoing.

- Phase II: 3 additional sites have opened protocol GU09-145 at the time of this analysis.

- Phase III: 434 patients have been enrolled to date.

- 29 of 283 patients on BNC105P alone have progressed.

- 42 of 291 patients on BNC105P/everolimus have progressed.

- The previously identified MTD of BNC105P (16 mg/m²) was achieved.

- No thrombotic event and no significant cardiovascular events within 6 months of registration.

- No prior treatment with temsirolimus or everolimus in the phase II component.

- WBC >3.5 K/mm³.

- Corrected QT interval (QTc) ≤450 msec.

- Other

- Completable malignancy, including trial sites.

- C0 < upper limit of normal.

- Complete blood count (CBC) with differential.

- Platelet count.

- Concomitant Medications

- Everolimus: 10 mg oral, daily

BNC105P: 4.2 mg/m²

BNC105P: 8.4 mg/m²

BNC105P: 12.6 mg/m²

BNC105P: 16 mg/m²

Everolimus: 10 mg oral, daily

PK analysis was performed on plasma BNC105P (in Everolimus+BNC105P) and plasma everolimus (in Everolimus alone) collected from phase I patients (Fig. 2). Sample collection was performed up to 8 h following administration of BNC105P in Cycle 1 (Days 1 and 8). Samples were collected into tubes containing 0.1 mg/mL of EDTA and stored at -80°C until analysis.

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