Final results from the first in human Phase I/II study of NUC-1031 in patients with solid tumours


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BACKGROUND

Prostate: Nucleotide Analogues
- A new class of anti-cancer agents
- Inhibitory phosphoribosyltransferase technology
- Overcome key cancer resistance pathways
- Broad clinical activity

NUC-1031: The First Anti-Cancer Prostate
- Overcome key cancer resistance mechanisms associated with prostate cancer
- C7H: a novel independent of androgen receptor (AR) inhibitor
- Activation independent of androgen-signaling (SAS) pathways
- Protective from estrogen disassociation inhibition (SAS)
- Greater stability
- Reduction in potentially toxic metabolites (SAS)

OBJECTIVES

- Primary
  a. Define recommended Phase II dose
  b. Assess safety profile
  c. Secondary
  d. Define PK and PD profiles
  e. Evaluate antitumour activity

Methods

- Sequential escalating cohorts (2-3 design) with NUC-1031 administered as a short 8-week infusion
- Schaalb (NUC-1031 administered at days 1, 8, 15 of a 4-week cycle (w/c))
- Schaalb (NUC-1031 administered on days 1, 8, 12, 15, 19 of a 4-week cycle (w/c))

Patient Population
- Patients aged >18 years with advanced, rapidly progressing, solid tumours refractory/refractory to all standard treatment

RESULTS

- 68 patients treated; 37 evaluable
- Median age 55 years (IQR 41-64)
- Average 2.7 prior chemotherapy regimens
- Primary tumour site: Prostate (72%), Lung (7), Colon (7), Breast (6), CUP (3), Endometrial (3), Melanoma (3), Osteosarcoma (3), Ovarian (2), Breast (2), Pancreatic (1), Bladder (1), Adenocarcinoma (1), Thymoma (1), Osteoblastoma (1)

Pharmacokinetics

- NUC-1031 plasma half-life is more favorable than gemcitabine (3-4 hours versus 1.5 hours respectively)

Safety

- No unexpected Adverse Events (AE)
- Most common AE: Grade 1 anemia, neutropenia, leucopenia
- Decreased WBC, neutrophils, lymphocytes
- 5 patients had Grade 4 AEs: metastatic esophagus, intestinal, atrial fibrillation, esophageal stricture, hypothyroidism
- 4 patients died of disease

Efficacy

- NUC-1031 achieved over 10x higher intracellular d4CPT levels than gemcitabine
- Gemcitabine

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- NUC-1031

Disease Control Rate (DCR)*

- All patients’ n
- Evaluable patients’ n

- Partial response
- 5
- 2
- 10
- 33
- 19

- Stable disease
- 30
- 19
- 79

*Estimated hazard ratio = 2.00

CONCLUSIONS

- NUC-1031: Novel prostate cancer drug
- Superior disease control in a high proportion of patients
- Durable PR of 4 months (longest)
- Activity in a broad range of cancers
- Disease control in patients refractory/unclassified to prior chemotherapy
- Gemcitabine
- Well tolerated with no unexpected AEs
- Demonstrates high intracellular levels of the active agent (d4CPT)
- Overcomes key cancer resistance mechanisms
- Molecular characterization may aid patient selection
- Phase II/III trials planned in ovarian, bladder and pancreatic cancers