The current Phase I study was initiated to determine the maximal tolerated dose of NKP-1339 when administered on a weekly schedule.

NKP-1339 is a small molecule that down-regulates the GRP78 pathway and reduces GRP78 levels in tumor cells.

Toxicity severity graded according to the CTCAE (ver. 3.0); occurring during Cycle 1 and related to NKP-1339:

- Definition of Dose Limiting Toxicity
  - No Peripheral neuropathy
  - No evidence of ischemia, recent MI, or significant abnormality on ECG
  - No symptomatic CNS metastases, no primary brain tumors
  - Adequate hematologic, hepatic and renal function
  - ECOG PS 0 or 1

Patients

Major Inclusion / Exclusion Criteria:
- Phase I study of single agent NKP-1339 infused over 60 minutes Days 1, 8 and 15 of 28-day cycle
- 18 years with histologically or cytologically confirmed advanced solid tumors refractory to standard therapies
doctaxel, sorafenib, bortezomib, etoposide, doxorubicin, temozolomide, vinblastine and camptothecins.

Background


NKP-1339: Maximum Tolerated Dose Defined for First-in-Man GRP78 targeted agent

- In cancer cells, the increase in malfolded proteins results in the accumulation of unfolded proteins in the ER, which stimulates the GRP78 pathway and the activation of anti-apoptotic pathways.
- GRP78 is translocated to the surface and extracellular space, nucleus, mitochondria, cytoplasm, cell membrane and extracellular matrix.
- In cancer cells with high levels of GRP78 in the ER lumen due to high levels of unfolded proteins, a translocation occurs out of the ER into the cytoplasm and mitochondria.
- In normal healthy cells, there is little GRP78 in the ER lumen due to low levels of unfolded proteins, resulting in low GRP78 levels in normal healthy cells.

Adverse Events

Most common adverse events occurring in ≥ 15% in the study population (N=46)

Enrollment

Study Design

Phase I study of single agent NKP-1339 infused over 60 minutes Days 1, 8 and 15 of 28-day cycle
Standard 3+3 design with Escalation Cutpoint to 25 patients at the MTD

Major Inclusion / Exclusion Criteria:
- ≥ 18 years with histologically or cytologically confirmed advanced solid tumors refractory to standard therapies
doctaxel, sorafenib, bortezomib, etoposide, doxorubicin, temozolomide, vinblastine and camptothecins.

Efficacy

36 pts completed 1 cycle of therapy and are evaluable to assess antitumor activity due to insufficient tumor response for assessment of antitumor response. All patients had PD at study entry.

Pharmacodynamics

- NKP-1339 is a small molecule targeting the GRP78 pathway
- The MTD of single agent NKP-1339 is 625 mg/m2 days 1, 8, 15 Q 28 d
- NKP-1339 is generally well tolerated

Conclusions

- DLT, DLT level, dose escalation and reversible creatinine elevation
- All MTD, the most common NKP-1339 adverse events are nausea, vomiting, and fatigue
- NKP-1339 can be administered with dacarbazine, paclitaxel, and docetaxel

For more information, visit www.niikipharma.com

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Dose Limiting Toxicity

Toxicity severity graded according to the CTCAE (ver. 3.0); occurring during Cycle 1 and related to NKP-1339:

- Grade 1 nausea/vomiting for 2 days
- Grade 2 hyperemesis or Grade 3 toxicity
- Grade 2 neuropathy
- Grade 2 nephrotoxicity
- Grade 2 neurotoxicity
- Grade 2 cardiotoxicity

NKP-1339 does not detectable in normal tissues. These preliminary results show that NKP-1339 could be well tolerated in patients treated at the MTD.

Pharmacokinetics

NKP-1339 has demonstrated activity in patients across tumor types, including NET and NSCLC patients.

Phase II trials in NET and Phase I combination chemotherapy trials are in development.