SINGAPORE 2017 ESMO ASIA

NOXOPHARM

NOX66 PLUS CARBOPLATIN

- Phase 1 Signalling Study

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DISCLOSURE SLIDE

The Authors are employees of the Sponsor Company, Noxopharm Limited

ABOUT NOX66

First-in-class inhibitor of tumour cell sphingosine kinase

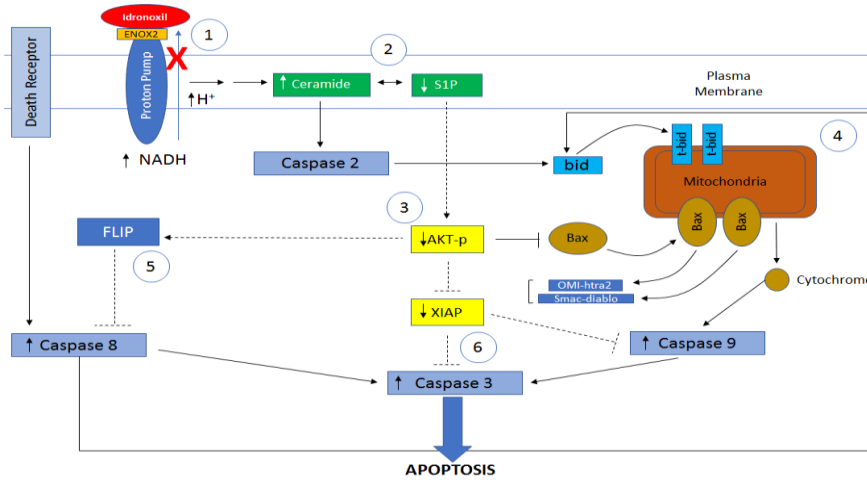
Idronoxil – inhibitor of external NADH oxidase–type 2 (ENOX2). *Oncogene*

- Inhibits sphingosine kinase
- Inhibits pro-survival signalling (S-1-P, Akt, PI3K)
- Inhibits DNA repair (PARP-1, topoisomerases 1 and 2)

Oral/IV dosage forms of idronoxil ineffective due to Phase 2 metabolism

NOX66 formulated as idronoxil in a hydrogenated fatty acid

- Blocks Phase 2 metabolism
- Creates 'pro-drug' form
- Improved drug-like features



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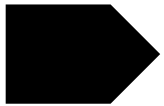
ABOUT NOX66

First-in-class inhibitor of tumour cell sphingosine kinase

Primary development as radio-sensitiser

- **External beam radiotherapy**
- **Brachytherapy (LuPSMA)**



- ❑ Increased response in irradiated lesions
- ❑ Abscopal response in non-irradiated lesions

Supplementary development as chemo-sensitiser

- ❑ Adjunct Rx with radiotherapy

RATIONALE

Idronoxil inhibits DNA repair following exposure to alkylating agents *(tumor cells only)*

Potent (10^3-10^4 x) sensitiser of carboplatin *in vitro*

? Increase response to carboplatin

? Allow carboplatin dose to be reduced

STUDY DESIGN

Phase: Phase 1, open label study

Patients: End-stage disease , metastatic solid tumours, no remaining standard treatments options

No. patients: 17 patients, 2 cohorts (400 mg and 800 mg NOX66).

1⁰ objectives: Safety. PK.

2⁰ objectives: Efficacy (RECIST) 3 and 6 months; ECOG Score; Biomarkers

Cohort 1: NOX66 400mg (Patients 1-8)	**RUN-IN** NOX66 MONOTHERAPY days 1-14	**+ CARBOPLATIN AUC=4** 3 x 28 Day cycles NOX66 days 1-7 Carboplatin Day 2	**+ CARBOPLATIN AUC=6** 3 x 28 Day cycles NOX66 days 1-7 Carboplatin Day 2
Cohort 2: NOX66 800mg (Patients 9-16)			
Replacement: NOX66 800mg (Patients 17-19)			

KEY INCLUSION / EXCLUSION CRITERIA

NOXOPHARM

Tumour types = Breast, Lung, Head & Neck, Prostate, Ovarian

KEY Inclusion criteria	KEY Exclusion criteria
Histologically confirmed locally or metastatic advanced solid tumours	Tumour involvement Central Nervous System
At least 1 measurable lesion on CT or MRI scan	Patients who are breastfeeding or pregnant
ECOG performance scale of 0-1	Clinically significant uncontrolled cardiac disease or myocardial infarction within last 12 months; QTc of >470 msec on screening ECG
Adequate heamatologic, hepatic and renal function	Uncontrolled infection or systemic disease
Minimum life expectancy of 12 weeks	Any major surgery, radiotherapy, immunotherapy within the last 21 days (palliative radiation > 2 weeks permitted
Fertile patients agree to use of effective contraception during study and 90 days after last dose of NOX66	No concurrent chemotherapy or biologic therapy; chemotherapy with delayed toxicity within last 4 weeks
	History solid organ transplant
	Known unsuitability for treatment with carboplatin or suppository use

INTERIM RESULTS

Data available at 16th November 2017

Fully enrolled:

16 patients recruited originally:

- Cohort 1 – 8 patients NOX66 400 mg
- Cohort 2 – 8 patients NOX66 800 mg

- 2 voluntary withdrawals (1 each Cohort); 1 SAE withdrawal
- 3 replacement patients enrolled and added to Cohort 2
  - *Final* Cohort 1 – 7 patients
  - *Final* Cohort 2 – 10 patients

INTERIM RESULTS

Data available at 16th November 2017

RUN-IN (Phase 1a) Arm. NOX66 monotherapy. 14 consecutive days.

Cohort 1. 8/8 completed

Cohort 2. 7/8 completed. *1 patient voluntary withdrawal*

No AEs reported

INTERIM RESULTS

Data available at 16th November 2017

PHASE 1b. NOX66 + LOW-DOSE (AUC4) CARBOPLATIN

Cohort 1. All 7/8 completed (*1 voluntary withdrawal*); 2 non-evaluable disease

Cohort 2. 5/10 completed. (5 yet to complete)

Safety: No SAEs reported

RECIST:

Cohort 1. 4/5 stable disease; 1/5 PD; (+ *2 non-evaluable*)

Cohort 2. 4/5 stable disease; 1/5 partial response

INTERIM RESULTS

Data available at 16th November 2017

PHASE 1b. NOX66 + HIGH-DOSE (AUC6) CARBOPLATIN

Cohort 1. 1 completed

Cohort 2. 0 completed.

Safety: 1 SAE reported (infusion reaction)

RECIST:

Cohort 1. 1/1 stable disease after 6 months. *6 current*

Cohort 2. *4 current*

PRELIMINARY CONCLUSIONS

- NOX66 well tolerated
  - No Adverse Events considered related to NOX66 use
  - No SAEs with NOX66 + carboplatin (AUC=4) after 3 cycles

- After 3-months with NOX66 + carboplatin (AUC4):
  - 9/11 patients with SD
  - 1/11 patients with PR
  - 1/11 Patients with PD
- Preliminary data suggest NOX66 in combination with low-dose carboplatin may benefit patients who are resistant to or unable to tolerate standard dose carboplatin.