Date: 13 November 2017 **Sydney, Australia**

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Noxopharm making three presentations at COSA

Sydney, 13 November 2017: Noxopharm is pleased to release the 3 presentations being made today at the Annual Scientific Meeting of the Clinical Oncology Society of Australia.

Two presentations concern the Company's clinical study being conducted in Georgia and now full recruited. A secondary aim of this study is to determine if blood levels of the active drug, idronoxil, and one of its target protein, ENOX2, might prove effective biomarkers in predicting drug efficacy and safety. Today's presentations are preliminary reports on the successful establishment of the two assays.

An update on the clinical response and safety data will be made to the ESMO (Asia) conference in Singapore on 18th November, 2017.

The third presentation concerns the clinical trial design of the Company's PROCART (Prostate Cancer Radio-sensitising Therapy) study to be conducted in 5 Australian radiation oncology centres, and currently recruiting and screening patients.

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About Noxopharm
Noxopharm is an Australian drug development company with offices in Sydney and Hong Kong. The Company has a primary focus on the development of drugs to address the problem of chemotherapy- and radiation-resistance in cancer cells, the major hurdle facing improved survival prospects for cancer patients. NOX66 is the first pipeline product, with later generation drug candidates under development. The Company also has initiated a pipeline of non-oncology drugs.

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ENOX2 levels of patients receiving NOX66

Ian Minns, Sue Khouri, Marinella Messina and Graham Kelly

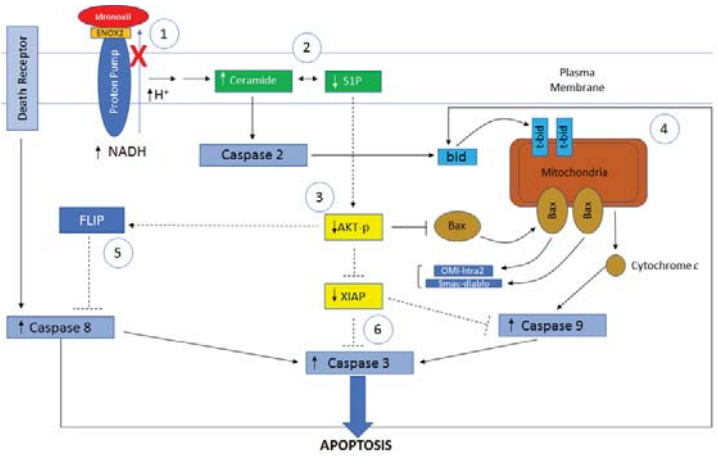
INTRODUCTION

The ECTO-NOX, or ENOX, proteins are a family of NAD(P)H oxidase proteins present on the cell surface of plants and animals. These proteins have two known and distinct biochemical activities, namely hydroquinone (NAD(P)H) oxidation and protein disulphide-thiol interchange, and are believed to play an important role in cell growth. In its constitutive form (CNOX, or ENOX1) these activities oscillate consistently at 24 min intervals. A second form of ENOX (tNOX, or ENOX2) has been identified, which has been found to be expressed on tumour cell surface and detected in sera of cancer patients[1]. Whilst ENOX2 performs the same dual function as ENOX1, the oscillation between functions occurs at 22 min intervals. From this, it is hypothesised that ENOX2 represents an important role in tumour cell growth and proliferation[2].

Importantly, while ENOX1 is refractory to quinone site inhibitors, the activity of ENOX2 may be suppressed by such inhibitors. It is this property which has led to investigation of ENOX2 inhibition as a target for anti-cancer therapy and the development of the isoflavone compound Idronoxil as a first-in-class inhibitor of ENOX2. The imputed pathway of ENOX2, and the mechanism by which inhibition of ENOX2 by Idronoxil may directly (via apoptosis) and indirectly (in combination with chemotherapy and / or radiotherapy via inhibition of DNA repair mechanisms) is outlined in Figure 1.

The compound NOX66, is a novel formulation and delivery mechanism for Idronoxil and is under clinical investigation for use in combination with standard chemotherapy and radiotherapy. The first-in-human study of NOX66, as a monotherapy (for safety evaluation) and in combination with carboplatin, is currently ongoing. Sixteen (16) patients with late stage metastatic disease (of primary origin prostate, lung, breast or ovarian) receive one of two doses of NOX66 (400mg, 800mg) as monotherapy (for 14 consecutive days) followed by low dose (AUC4) carboplatin for 3 x 28-day cycles and standard dose (AUC6) carboplatin for 3 x 28-day cycles. This poster presents interim results for the analysis of plasma ENOX2 levels in this cohort of patients.

Figure 1. Putative biochemical pathway associated with idronoxil.



The cascade of events outlined above is as follows[2-5]:

1. Idronoxil binds to ENOX2, leading to inhibition of the trans membrane electron pump which, in turn, leads to an accumulation of proton ions within the plasma membrane.
2. Accumulation of protons disrupts sphingomyelin pathway with blockage of ceramide conversion to S1P – leading to a decrease in S1P and an increase in Ceramide within the plasma membrane.
3. Decrease of S1P leads to a reduction in PI3K, Akt and XIAP and an increase in Caspase 2.
4. Reduction in Akt leads to reduction in NF-κB and allows up regulation of the intrinsic (mitochondrial) pathway of apoptosis, via an increase in Caspase 9 and Caspase 3, leading to cell death.
5. Reduction in Akt also results in an inhibition of FLIP resulting in an increase in Caspase 8 (activated via the Death Receptor on the Protein Membrane) – leading directly and indirectly (via the intrinsic pathway) to an increase in Caspase 3 and apoptosis.
6. Reduction in XIAP prevents down regulation of Caspase 9 and Caspase 3, supporting apoptosis.

METHODS

Samples for analysis were collected from patients participating in the study "NOX66-001: Safety, PK and Efficacy of NOX66 as a Monotherapy and Combined with Carboplatin in Refractory Solid Tumours" (ClinicalTrials.gov identifier NCT02941523). Commercially available lung and prostate tumour plasma controls were used as reference for qualitative review and non-tumour plasma was used as negative control.

Determination of plasma ENOX2 levels was conducted at Crux Biolab, Melbourne, Victoria, using the Human Ecto-NOX Disulfide-Thiol Exchanger 2 (ENOX2) ELISA Assay. This assay employs a quantitative sandwich linked immunoassay sorbent procedure with microplates pre -coated with an antibody specific to ENOX2. Following exposure of a sample to the antibody, any unbound substance is removed and a biotin-conjugated antibody (specific for ENOX2) is added. Avidin-enzyme conjugated horseradish peroxidase is introduced, followed by a substrate solution initiating colour development then an acid based solution is used to stop the reaction. Colour intensity is measured and correlated to ENOX2 concentration (pg/mL). In order to assess samples within the range of the assay, control samples were diluted 5-10-fold and patient samples analysed at 5-fold dilution. All samples were analysed in duplicate.

RESULTS

Figure 2. ENOX2 levels of control tumour plasma samples (measured by 5x and 10x dilution)

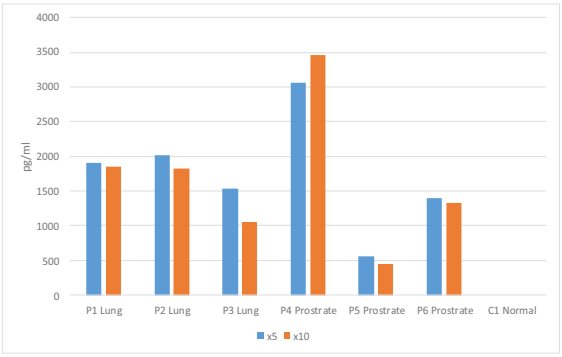
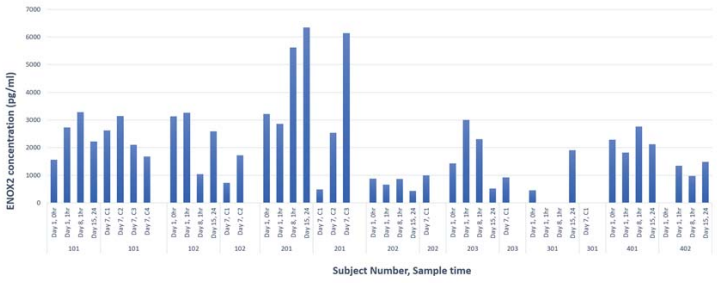


Figure 3. ENOX2 levels of patient samples, NOX66-001 study



CONCLUSION

The human ENOX2 ELISA assay allows for the measurement of ENOX2 in human plasma samples.

Intra-patient comparison of plasma ENOX2 shows variation in concentrations between samples, suggesting that shedding of ENOX2 protein may not remain consistent and indirect measurement of ENOX2 via plasma concentrations may not provide a quantitative assessment of ENOX2 activity.

Further validation of the ELISA based ENOX2 assay, and direct analysis of tumours (e.g. via biopsy) are required to allow relationship of ENOX2 level and efficacy of NOX66 to be assessed.

REFERENCES

1. Cho et al (2002). "Monoclonal antibody to a cancer- specific and drug-responsive hydroquinone (NADH) oxidase from the sera of cancer patients". Cancer Immunol. Immunother. Vol 51 (3); pp 121–129
2. Morre and Morre (2003). "Cell Surface NADH Oxidases (ECTO-NOX Proteins) with Roles in Cancer, Cellular Time-Keeping, Growth, Aging and Neurodegenerative Diseases". Free Rad. Res. Vol 37 (8); pp 795-808
3. Morre et al (2007). "ECTO-NOX Target for the Anticancer Isoflavene Phenoxodiol." Oncol Res. Vol 16; pp 299-312
4. De Luca et al (2008). "Downstream Targets of Altered Sphingolipid Metabolism in Response to Inhibition of ENOX2 by Phenoxodiol." Biofactors. Vol 34 (3); pp 253-260
5. Huang et al (2011). "Roles of Sphingosine-1-Phosphate on Tumorigenesis" World J. Biol. Chem. Vol 2 (2); pp 25-34

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Financial Disclosures: The authors are employees of Noxopharm Limited, the sponsor company of this study

Idronoxil levels of patients receiving NOX66

Ian Minns, Marinella Messina and Graham Kelly

BACKGROUND

The experimental anti-cancer drug Idronoxil is a first-in-class inhibitor of the oncogene external NADH oxidase Type 2 (ENOX2). ENOX2 maintains the trans-membrane electron potential (TMEP) of the cancer cell plasma membrane, with loss of TMEP disrupting a wide range of functions of the plasma membrane. Inhibition of sphingosine kinase is a major outcome, resulting in loss of a range of pro-survival signalling pathways, notably PI3K and Akt, and consequent loss of function of DNA repair enzymes including PARP 1 and topoisomerases 1 and 2.

Idronoxil was previously investigated as a chemo-sensitiser, utilising its ability to block repair of DNA damage in order to optimise chemotherapy-induced tumour damage whilst minimising non-tumour toxicity. In vitro and in vivo (mouse xenografts) data have shown that idronoxil sensitises by up to 2000-fold the cytotoxic effects of standard cytotoxic drugs including cisplatin, carboplatin, paclitaxel, gemcitabine, toptecan, doxorubicin and captothecin.

Promising early phase results led to a Phase 3 study of oral idronoxil as a sensitiser of carboplatin in patients with carboplatin-refractory ovarian cancer, however this study was discontinued early with data showing no improved efficacy with idronoxil. Subsequent review of the mechanism of action of idronoxil suggested that, for significant biological effect, a constant presence of the parent drug must be present. With a short elimination half life and extensive Phase 2 metabolism in oral and IV formulations, administration of idronoxil in standard form is unsuitable as a drug candidate.

NOX66 is under development as a formulation of idronoxil, specifically designed to overcome the issues identified with oral and IV formulation. Pre-clinical investigations in rats (Table 1) show that NOX66 delivered rectally leads to an extended elimination half life of parent drug in comparison with IV idronoxil.

A first-in-human study of NOX66 as monotherapy and in combination with carboplatin was commenced in March 2017, with preliminary results presented at the ESMO Annual Scientific Meeting in September (summarized below). As part of this study, plasma and urine samples are collected to review and assess the detectable levels of parent idronoxil in patient plasma and urine. Here we outline the assay method, and preliminary finding for monotherapy samples.

Table 1: Comparison of pharmacokinetic parameters of idronoxil administered intravenously in a lipid-free co-solvent formulation and rectally administered NOX66 in rats (n=4 per arm).

Parameter:	IV idronoxil	NOX66 (rectal)
Dose (mg/kg)	3.5[a]	35
Cmax (ng/mL)	4647 ± 315	62.3 ± 8.7
Tmax (h)	-	0.12 ± 0.04
$AUC_{0\text{-}30}$ (ng.h/mL)	8129 ± 166	1187 ± 389
Half-life (h)	0.32 ± 0.07[b]	9.6; 6.1[c]
Bioavailability (%F from 0-30h)	100	14.6 ± 4.8

[a] 3.5 mg/kg administered, however PK parameters have been normalised to equivalent of 35 mg/kg

[b] Half life estimate using values from 0.17h. No measurable drug was seen in any rat beyond 2h

[c] Values for 2 rats only

ANALYTICAL METHOD

Plasma and 24h urine samples from 8 patients receiving NOX66 (400mg) were collected and extracts prepared using protein precipitation with acetonitrile then analysed at HMSTrust Laboratory, Monash University. LC-MS analysis was performed on a Shimadzu 8050 triple quadrupole instrument coupled with a Shimadzu Nexera X2 UHPLC. An internal standard of diazepam was used in all samples.

RESULTS

Figures 1-4 show representative chromatograms of control human plasma and standard solvent and of representative plasma and urine extracts from cohort 1 patients.

Chromatograms show internal standard diazepam peak, parent idronoxil peak and metabolite peaks in patient extracts only.

All urine samples analysed have shown detectable levels of parent drug (idronoxil) and metabolites, whilst parent drug was consistently detected in six of eight patients' plasma samples, with all showing evidence of metabolites. Table 2 shows Idronoxil levels measured in plasma (Day 1, 2 hours post NOX66 administration and Day 8, prior to next NOX66 administration) and urine (24h sample from Day 1)

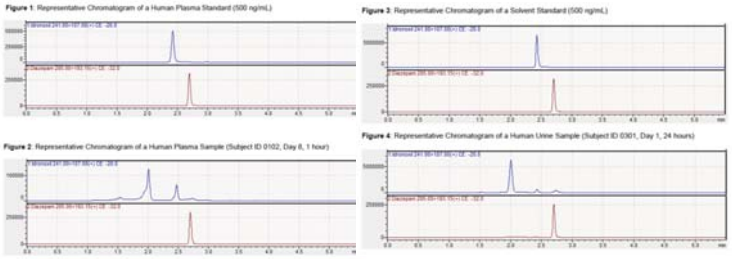

Table 2: Parent idronoxil levels of patients receiving NOX66 400mg.

Plasma samples were collected at 2 hours following administration of first dose of NOX66, and prior to next dose administration on Day 8. post 7 days of consecutive daily NOX66 dosing) 24h Urine sample was collected across Day 1 of administration of NOX66 .

Subject Number	101	102	201	202	203	301	401	402
Patient No.	1	2	3	4	8	5	6	7
Plasma Idronoxil: Day 1, 2h (ng/mL)	6.7	25.2	ND	22.1	15.0	ND	<LLOQ	24.9
Plasma Idronoxil: Day 8, 0h (ng/mL)	5.7	26.4	ND	24.2	9.5	ND	ND	26.9
Urine Idronoxil[a]: Day 1 24h (µg/mL)	0.59	0.22	<LLOQ	0.03	0.05	0.95	0.24	0.20

LLOQ = Lowest Level of Quantification; ND = Not Detected

CONCLUSION

Parent idronoxil can be detected using LC-MS analysis in patients receiving 400mg NOX66 daily, with initial data suggesting a constant presence of parent drug and minimal accumulation. Further PK studies are required to confirm initial findings. Development and confirmation of this method allows for further determination of idronoxil and its metabolites in relation to response to treatment with NOX66.

NOX66-001 Study Overview and Interim Findings

(Presented at ESMO, September 2017)

NOX66-001 STUDY - INTERIM DATA FOR COHORT 1

Pt	Tumour Type	Monotherapy (21 day cycle) Phase 1a Status	Combination Therapy (28 day cycles) Phase 1b Status	Response#(Cycle 3) Target Lesion RECIST 1.1 criteria	Adverse Events (Phase 1B) ALL	Severity*	Related to NOX66
1	Ovarian	Complete	Ongoing - Cycle 6	Stable Disease Stable disease (Cycle 6)	Nausea	Grade 1/mild	UR
2	Lung	Complete	Withdrawn	Progressive Disease	NIL		
3	Lung	Complete	Ongoing - Cycle 4	Stable Disease	Pulmonary embolism Arterial embolism	Grade 1/mild Grade 1/mild	UR
4	Lung	Complete	Withdrawn (pt decision)	ND			
5	Breast	Complete	Ongoing - Cycle 4	Stable Disease	Exudative pericarditis Bilateral hydrothorax WBC elevation	Grade 1/mild Grade 2/mod Grade 2/mod	UR
6	Breast	Complete	Ongoing - Cycle 3	ND	Hypocalcaemia	Grade 2/mod	UR
7	Breast	Complete	Ongoing - Cycle 3	ND	Asthenia Peripheral neuropathy	Grade 2/mod Grade 1/mild	UR
8	Prostate	Complete	Ongoing - Cycle 3	ND	NIL		

*# First response assessment by Investigator; * NCTCAE v4.03 ; ND=Not Determined; UR= unrelated*

- Phase I open label, 2 -step dose escalation study of NOX66, a suppository formulation, in patients with refractory solid tumours.
- Tumours selected for 5 phenotypes: breast, head and neck, lung, prostate and ovarian.
- Total 16 evaluable patients: n=8 allocated to 400mg NOX66 dosage Cohort 1; n=8 allocated to 800mg dosage Cohort
- The study comprises 2 stages of assessment:
  1. Monotherapy: NOX66 is administered for daily for 14 consecutive days
     - plasma and urine samples collected throughout
  2. Combination therapy: NOX66 plus IV Carboplatin
     - Up to 6 x 28 day cycles; NOX66 Days 1-7, Carboplatin Day 2
     - Cycles 1-3 = Low Dose (AUC4); Cycles 4-6 = Standard Dose (AUC6)
- Patient assessed for safety parameters
- Preliminary response on CT images by investigator per RECIST 1.1 at 3 months (Cycle 3) and 6 months (end cycle 6)
- Replacement of non-evaluable patients is permitted

Financial Disclosures: The authors are employees of Noxopharm Limited, the sponsor company of this study

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Trial Design: Safety of NOX66 in Combination with Palliative Dose Radiotherapy - A Phase 1 Dose Escalation Study

Ian Minns, Marinella Messina and Graham Kelly

Background

The experimental anti-cancer drug Idronoxil is a first-in-class inhibitor of the oncogene external NADH oxidase Type 2 (ENOX2). Inhibition of ENOX2 in tumour cells can cause a cascade of events which ultimately promote cell apoptosis and prevent DNA repair in damaged cells.[1-4] It has further been shown *in vitro* that inhibiting Sphingolipid metabolism, which can be achieved through ENOX2 inhibition, can enhance the effect of radiation in causing cell injury and death.[5-6]

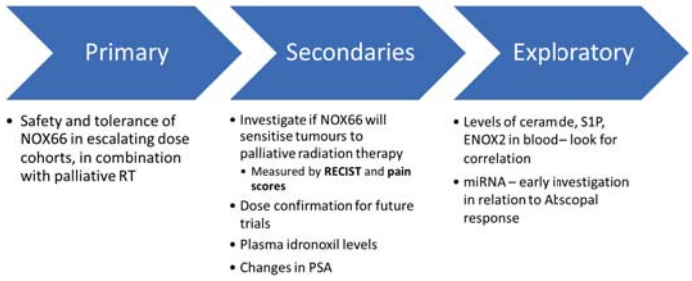
NOX66, a novel formulation containing Idronoxil as an active ingredient and designed for rectal administration, is under clinical investigation in combination with chemotherapy and radiotherapy. It is hypothesised that NOX66, through delivery of Idronoxil to tumour cells and inhibition of ENOX2, may enhance the effects of radiotherapy in target tumours and provide improved efficacy in irradiated tumours. Furthermore, the Idronoxil-ENOX2 interaction may facilitate the stimulation of an abscopal response within non-irradiated tumour cells due to the direct pro-apotosis effects of Idronoxil. Here we describe the design of the first-in-human study of NOX66 in combination with radiotherapy in patients with late-stage prostate cancer, investigating the safety of three dose levels of NOX66.

Study Title: NOX66 and Palliative Radiotherapy in Patients with Late-Stage Prostate Cancer - A Phase 1b Proof of Concept and Dose Confirmation Study

ClinicalTrials.gov Identifier: NCT03307629

KEY Inclusion criteria
Histologically confirmed prostate cancer and/or PSA of >100 ng/mL at original diagnosis
Metastatic disease evidenced by either CT/MRI imaging or bone scan
Objective evidence of disease progression
Eligible to receive palliative radiation therapy for management of disease
At least two lesions, one of which is measurable and one which is suitable for radiation therapy
Ongoing androgen deprivation therapy with luteinizing hormone-releasing hormone (LHRH) agonist or antagonist
ECOG Performance status 0-2
KEY Exclusion criteria
Tumour involvement of the central nervous system
Concurrent systemic chemotherapy or biological therapy.
Any situation where the use of suppository therapy is contra-indicated or impractical (eg.

Study Objectives



Study Methodology

A total of 24 patients will be recruited into the trial, in four cohorts

- Cohort 1 (n=4): NOX66 400mg
- Cohort 2 (n=4): NOX66 800mg (subject to dose escalation criteria being met)
- Cohort 3 (n=4): NOX66 1200mg (subject to dose escalation criteria being met)
- Cohort 4 (n=12): NOX66 dose to be determined from assessment of cohorts 1-3

The Study will involve treatment with NOX66 and radiation therapy as follows:

Baseline: Tumour assessment scan using CT/MRI, screening laboratory assessments (including PSA levels), and pain assessment (Brief Pain Inventory-Short Form)

Day 1-15: NOX66 will be administered rectally (one, two or three suppositories daily, depending on cohort allocation)

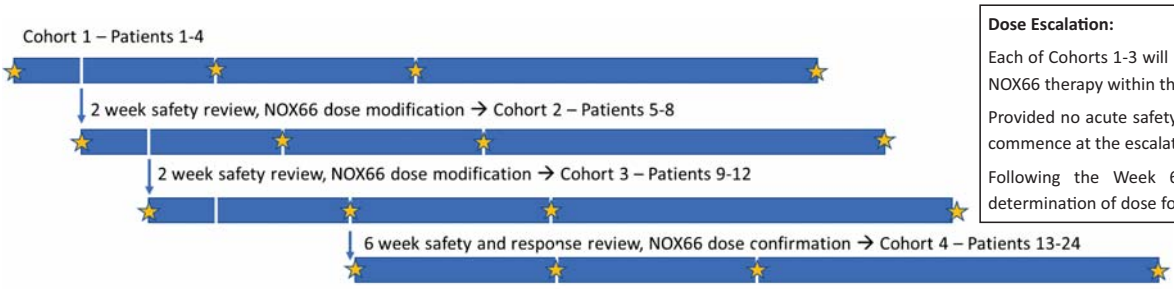
Day 2-8: Lesions selected for irradiation will receive palliative dose (20Gy) radiation therapy in 5 fractionated doses over 7 days (no radiation therapy on weekends).

Week 6: Initial follow up scan using CT/MRI, follow up laboratory assessments (including PSA levels), and pain assessment

Week 12: Second follow up scan using CT/MRI, follow up laboratory assessments (including PSA levels), and pain assessment

Week 24: third follow up scan using CT/MRI, follow up laboratory assessments (including PSA levels), and pain assessment

Patients will continue to be followed up after 24 weeks at the discretion of the investigator.



Dose Escalation:

Each of Cohorts 1-3 will be reviewed following the completion of NOX66 therapy within the cohort (4th patient, Day 15).

Provided no acute safety signals are noted, the next cohort shall commence at the escalated dose.

Following the Week 6 Scan for patient 12 (cohort 3) a determination of dose for cohort 4 will be made

References

1. Morre and Morre (2003). "*Cell Surface NADH Oxidases (ECTO-NOX Proteins) with Roles in Cancer, Cellular Time-Keeping, Growth, Aging and Neurodegenerative Diseases*". Free Rad. Res. Vol 37 (8); pp 795-808
2. Morre *et al* (2007). "*ECTO-NOX Target for the Anticancer Isoflavene Phenoxodiol.*" Oncol Res. Vol 16; pp 299-312
3. De Luca *et al* (2009). "*Downstream Targets of Altered Sphingolipid Metabolism in Response to Inhibition of ENOX2 by Phenoxodiol.*" The Prostate. Vol. 70; pp 1211-1221
4. Huang *et al* (2011). "*Roles of Sphingosine-1-Phosphate on Tumorigenesis*" World J. Chem. Pp 25-34
5. Rodriguez-Lafrasse *et al* (2002). "*Increasing Endogenous Ceramadie Using Inhibitors of Sphingolipid Metaboilism Maximizes Ionizing Radiation-Induced Mitochondrial Injury and Apoptotic Cell Killing.*" Int. J. Cancer. Vol 101; pp589-598
6. Kolesnick and Fuks (2003). "*Radiation and Ceramide Induced Apoptosis*" Oncogene. Vol 22; pp 5897-5906

Study Locations

The Study is being conducted at Radiation Oncology Centres in NSW and Queensland

Acknowledgement

This trial is being conducted in collaboration with TROG Cancer Research Australia

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Financial Disclosures: The authors are employees of Noxopharm Limited, the sponsor company of this study