
Nyrada ASX Announcement – Oncology Study Update

Company Update – 23rd August 2026

Results from a pre-clinical study, released to the market last Friday (21st August), have shown that Xolatrip protected cardiac function from progressive doxorubicin-induced toxicity with benefits across four key measures of heart performance. The results pave the way for Xolatrip to enter a human clinical trial in oncology.

BACKGROUND INFORMATION

Anthracyclines, including doxorubicin, are a highly potent class of chemotherapy drugs used to treat many types of cancers including breast cancer, lymphomas, and sarcomas. The limiting factor in using these drugs is cardiotoxicity leading to significant and permanent damage that affects the heart's ability to function normally. It is important to note that cardiac injury is both dose-dependent and cumulative. The development of anthracycline-induced cardiac dysfunction can ultimately necessitate dose reduction, treatment interruption, or discontinuation of an otherwise effective anticancer therapy.

Doxorubicin has been used as a "backbone drug" in oncology since the 1970s. Dexrazoxane is an established cardioprotective agent which has been used to provide protection from the toxicity caused by chemotherapy drugs. However, its use is not routine across the broader population of patients receiving drugs like doxorubicin due to limitations in approved indications, concerns regarding potential effects on anticancer efficacy and secondary malignancies, and additional haematological toxicity [to the blood or blood forming tissues]. Current cardio-oncology guidelines support consideration of using dexrazoxane particularly in patients receiving high cumulative chemotherapy doses, which causes cardiotoxicity, or those at high or very-high cardiovascular risk.

There remains a significant unmet clinical need for cardioprotective therapies that can be used alongside chemotherapy to reduce cumulative cardiac injury while preserving the anticancer efficacy of treatment.

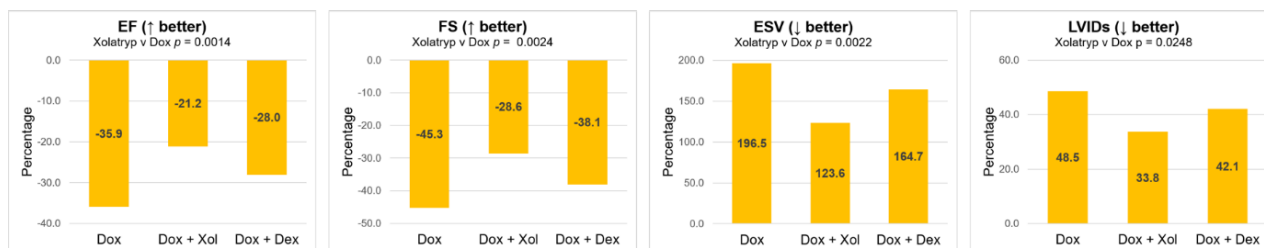
STUDY RESULTS

In this study, Xolatrip was assessed against doxorubicin with dexrazoxane being used as a positive control. The study showed that treatment with doxorubicin weakened the heart's ability to pump blood effectively. The heart squeezed less strongly, as shown by lower ejection fraction (EF) and fractional shortening (FS), and more blood remained in the heart after each beat, shown by increased end-systolic volume (ESV) and a larger heart chamber size during contraction (LVIDs). Overall, these changes indicate reduced heart pumping function.

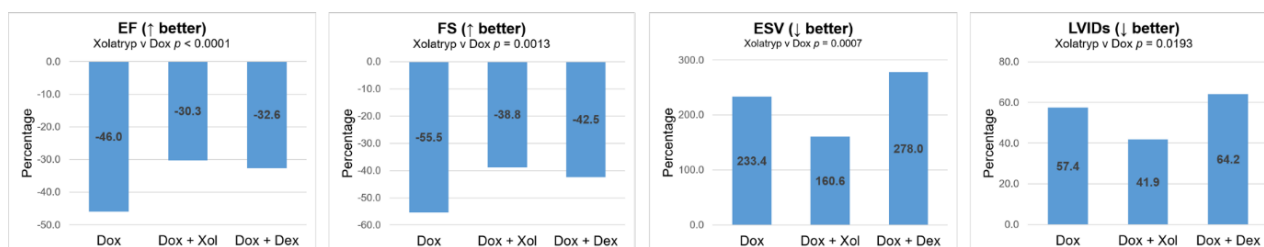
Animals receiving Xolatrip showed significantly improved heart function across EF, FS, ESV and LVIDs. Protection was statistically significant across each parameter at Week 3 and was sustained through Week 5, by which point doxorubicin-induced dysfunction had progressed substantially. This longitudinal pattern is consistent with sustained cardioprotection rather than an effect confined to a single timepoint. The charts below show that functional cardioprotection with Xolatrip compared favourably with doxorubicin alone across all four systolic parameters. Echocardiographic measures of cardiac function are generally accepted by regulators as clinically meaningful endpoints, which supports the relevance of these findings to a future clinical programme.

Week 3 review (orange) and week 5 review (blue)

Week 3



Week 5



Values represent mean percentage change from baseline.
 ↑/↓ indicates the direction associated with better cardiac function.

Functional cardioprotection with Xolatryp compared to that observed with dexrazoxane (see table below) showed that mean changes numerically favoured Xolatryp across all four systolic parameters. All four parameters reached statistical significance versus doxorubicin alone at both timepoints, meaning the improvements observed are unlikely to have arisen by chance.

Mean percentage change from baseline in key echocardiographic parameters at week 3 and week 5

Parameter	Time	Doxorubicin	Xolatryp + Doxorubicin	Dexrazoxane + Doxorubicin	Xolatryp protection vs Doxorubicin	Xol vs Dox p-value*
EF ↑ better	W3	-35.9%	-21.2%	-28.0%	41% less decline	0.0014
	W5	-46.0%	-30.3%	-32.6%	34% less decline	<0.0001
FS ↑ better	W3	-45.3%	-28.6%	-38.1%	37% less decline	0.0024
	W5	-55.5%	-38.8%	-42.5%	30% less decline	0.0013
ESV ↓ better	W3	+196.5%	+123.6%	+164.7%	37% less increase	0.0022
	W5	+233.4%	+160.6%	+278.0%	31% less increase	0.0007
LVIDs ↓ better	W3	+48.5%	+33.8%	+42.1%	30% less increase	0.0248
	W5	+57.4%	+41.9%	+64.2%	27% less increase	0.0193

* Repeated-measures Two-way ANOVA with Holm-Sidak post hoc (n = 12 per group)

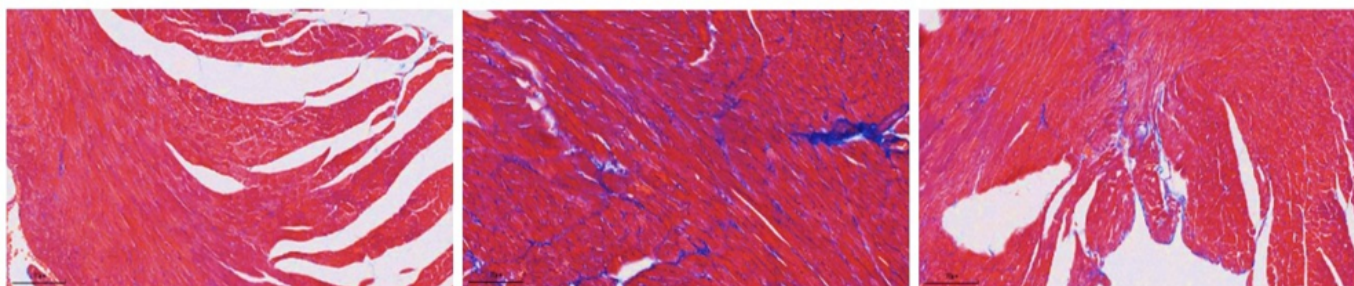
It is worth noting that the dosing schedules differed between the two treatment arms. Dexrazoxane must be administered before doxorubicin in order to work, and was therefore given 30 minutes prior. Xolatryp dosing began 10 minutes after doxorubicin. Since doxorubicin causes cardiac injury rapidly, dosing after the insult is a more conservative test than pre-dosing, when the protective agent would already be established in the body. Xolatryp nonetheless matched or numerically exceeded dexrazoxane across all four functional parameters.

Two supporting measures were also assessed. Cardiac troponin I, a marker of heart muscle cell injury, was reduced by approximately 19% at Week 5 relative to doxorubicin alone ($p = 0.0535$). Myocardial collagen content fell from 17.4% with doxorubicin alone to 13.2% with Xolatryp, a relative reduction of approximately 24%.

HISTOPATHOLOGICAL REVIEW SUPPORTIVE OF FUNCTIONAL RESULTS

Histopathological [tissue] examination, performed blinded, confirmed a clear doxorubicin-induced injury, comprising disordered myocardial fibres, focal myofiber rupture, widened intercellular spaces, interstitial oedema, and focal inflammatory-cell infiltration, with Masson's trichrome staining showing focal collagen proliferation and fibrotic lesions.

Results from trichrome-stained sections of rodent heart at the end of the 5-week study



Vehicle: Normal tissue

- Predominantly red muscle fibres
- Minimal blue collagen

Doxorubicin

- Moderate tissue injury
- Increased blue collagen deposition

Doxorubicin + Xolatryp

- Mild tissue injury
- Reduced blue collagen compared to doxorubicin alone

In the above images collagen [representing damaged tissue] stains blue and myocardium (normal heart muscle tissue) stains red. Doxorubicin treatment resulted in increased collagen deposition and myocardial injury compared with vehicle (normal). Co-treatment with Xolatryp (32 mg/kg) reduced collagen deposition and improved myocardial architecture.

Overall injury severity in Xolatryp-treated animals was reduced from predominantly moderate focal myocardial injury (damage to a medium-sized, localised area of the heart muscle) to predominantly mild focal injury (a small, localised area of heart muscle has suffered minor damage or stress), the same characterisation applied to the dexrazoxane positive-control group.

Nyrada previously reported preclinical data from a separate liver cancer tumour model in which Xolatryp showed anti-tumour activity as a single agent, and improved anti-tumour activity when combined with doxorubicin.

James Bonnar, Nyrada CEO, commented on the results “Combined with our previous finding that Xolatryp has anti-tumour activity and enhances the response to doxorubicin in a tumour model, we believe Xolatryp has the potential to offer an important new approach to anthracycline therapy, protecting cardiac function while preserving, and potentially enhancing, the anti-cancer effect.”

The results from this study clearly support the development of Xolatryp as an adjunct therapy with chemotherapy drugs in the oncology setting.

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