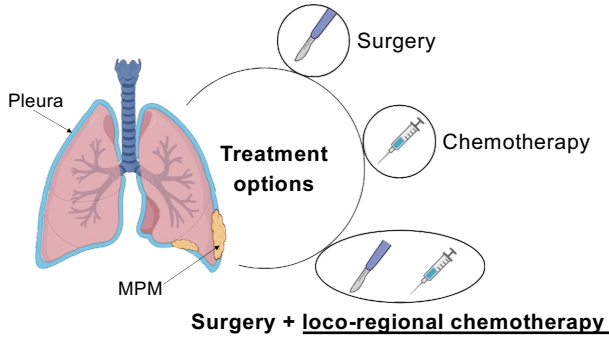


Cisplatin-loaded hyaluronan film for loco-regional chemotherapy: from technological development to preclinical evidence of activity

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MALIGNANT PLEURAL MESOTHELIOMA (MPM): UNCURABLE RARE CANCER



OUR STRATEGY FOR NOVEL ORPHAN MEDICINES: to repurpose approved drugs by innovative delivery systems!

HYALCIS FDA EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

- Novel orphan medicinal product, consisting in a hyaluronan (NaHA) film loaded with cisplatin (cisPt), for loco-regional drug delivery in MPM.
- Implanted in thorax during surgery for primary tumor resection to prevent or delay local metastases.



HYALCIS MILESTONES

Film technology

Composition: 1% cisPt, NaHA, PVA, sorbitol, PEG 200 and PEG 1000 stearate.

Characteristics: thickness, tensile strength, solid state (DSC, X-Ray), drug content, *in vitro* cisPt release.

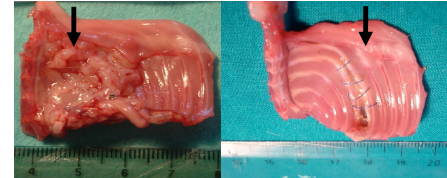
1st preclinical study on rats with MPM

HYALCIS applied on pleural cavity after MPM resection **WAS EFFECTIVE** compared to cisPt solution administered intravenously and intrapleurally.

Local metastases volume was reduced with no cisPt-related hematological toxicity!

cisPt SOLUTION

HYALCIS

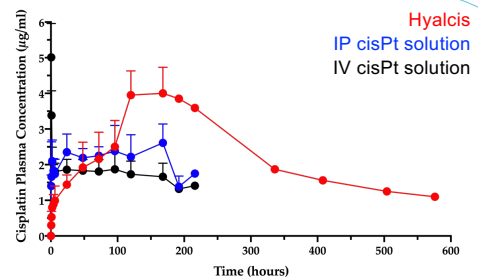


2nd preclinical study on healthy sheep for PK and toxicity assessment

HYALCIS prolonged cisPt release and plasma concentration was high compared to intravenous and intrapleural cisPt treatment.

Despite such high concentration, there were no cisPt-related hepatic and renal toxicity. Hence,

HYALCIS WAS SAFE!



Plasma concentrations of cisPt up to 9 days after treatment with HyalCIS and cisPt solution given intrapleurally (IP) or intravenously (IV).

Was HyalCIS safety due to a circulating complex formed between cisPt and NaHA?

PROOF OF COMPLEX

cisPt/NaHA (NANO)COMPLEX investigation

- ✓ Complex formation during film manufacturing and detection by HPLC.
- ✓ cisPt **complexation** by NaHA slows down its release from film (**prolonged effect**).
- ✓ cisPt/NaHA complex has the form of nanoparticles (123.3 ± 3.4 nm), possibly enabling lymphatic uptake *in vivo*.

THE FUTURE OF HYALCIS

- ❑ Detect the circulating complex in blood.
- ❑ Clinical development for MPM.
- ❑ cisPt/NaHA complex application in sensitive tumors (e.g. melanoma) in new dosage forms.