

Hamlet NEWSLETTER

Important steps forward towards treating bladder cancer

We are pleased to inform you that our clinical dose escalation study with the Hamlet peptide drug Alpha1H in patients with bladder cancer was successfully completed in December 2021. The data analysis is ongoing but the preliminary results communicated are very promising indeed.

We are also proud that despite the pandemic, we have completed the study on time, emphasizing our commitment to patients and shareholders.

This important step on the journey from discovery to a drug puts us closer to the final stages of drug development, before Phase III and FDA approval.

Each year around 500 000 patients worldwide are diagnosed with bladder cancer, which results in around 165 000 annual deaths. Bladder cancer has the highest recurrence rate of all cancer indications. This means that more than 80% recur after complete surgical removal of the first tumor and 15% progress to muscle invasive disease.

Patients have now been treated with Alpha1H, a synthetic drug candidate derived from HAMLET; the first in a family of cancer killing compounds with astonishing properties.

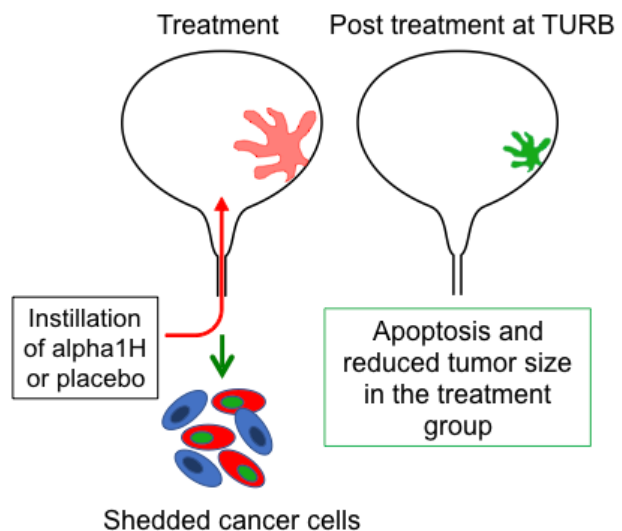
A dose escalation study like this is a fairly advanced step in a clinical trial program for a new drug. Drug development usually starts with a Phase I study, which is performed to ensure that the drug candidate is not too toxic for further development. Alpha1H has been extensively tested in animal models and found not to be toxic for the bladder. In the Phase I/II trial, there was no evidence of toxicity compared to the placebo group. In addition, positive effects on the tumor were documented, including cell shedding, a loss of cancer gene expression, apoptosis and a reduction in tumor size.

The purpose of a dose escalation study is to see if treatment with an increased dose of the drug candidate, results in increased effects in the patients.

This is precisely what happened.

The tumors were more strongly affected than in patients treated with the lower dose and compared to the placebo group.

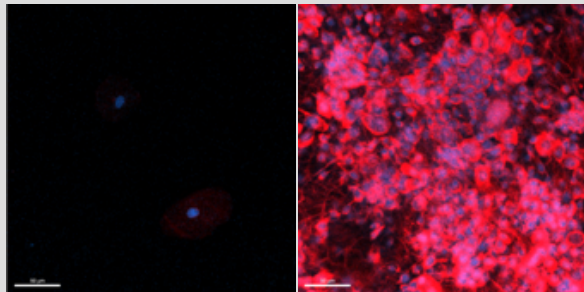
This correlation between dose and effect strongly indicate that the substance is behaving like a "real drug", and that it may be possible in the future to administer Alpha 1H according to the special needs of the individual patient.



Alpha1H has also the potential to be used to treat other cancer types as well. HAMLET kills more than 40 different types of tumor cells in the test tube, including those, which are difficult to treat with available drugs.

About the study

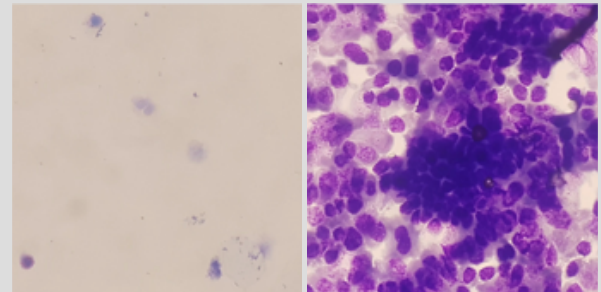
The patients were given Alpha1H or placebo directly into the bladder. By comparing urine samples from before and after the treatment, we detect a substantial increase in tumor cell shedding among the patients receiving active substance, along with an accumulation of cells containing Alpha1H.



Before

After

Uptake of Alpha1H (red cells) in urine samples taken after treatment with Alpha1H. Tumor cells are shown to contain large amounts of Alpha1H after but not before treatment.

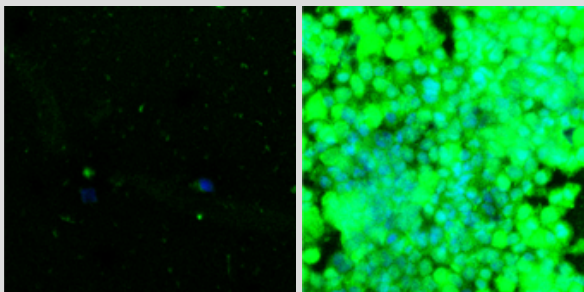


Before

After

Cancer cell shedding in urine samples taken after but not before the treatment with Alpha1H. Tumor cells and fragments are stained blue.

Within just two hours after the patient had received Alpha1H, we see an increase in cell death, so-called apoptosis. These effects were increased in patients treated with the higher dose of Alpha1H. At the time of surgery, major responses were observed in the tumors.

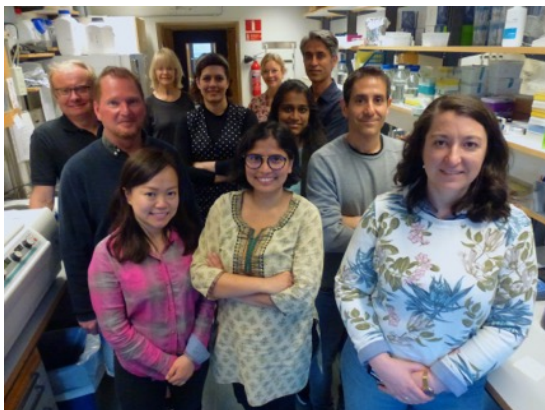


Before

After

Tumor cell death induced by Alpha1H. Large numbers of green, dying cells are seen in urine samples taken from the patients after treatment with Alpha1H.

Apoptosis is a beneficial, non-toxic form of cell death, and therapies inducing apoptosis in growing tumors are highly desirable to limit the side effects of cancer therapy. Apoptosis in itself is a natural process, and the average adult human loses between 50 and 70 billion cells each day due to apoptosis. Alpha1H appears to specifically target undesirable cancer cells, and kill them by this mechanism, which is much less toxic and painful than many other forms of cancer treatment.



The higher dose was also shown to shut down the engine of the tumor cells, where RNA is translated to new proteins. This means that Alpha1H does not just target one part of the tumor cell machinery, but has a general effect on essential tumor cell functions, limiting their growth and inducing cell death.

**Read more about
our work at hamletpharma.com**