Novel immunotherapeutic treatment for superficial Bladder Cancer

Summary

Bladder Cancer treatment usually combines chemotherapy agents and immunotherapy comprising the intravesical administration of *Mycobacterium bovis* BCG (TheraCys).

The administration of BCG shows a direct cytotoxic effect on tumor cells and also triggers a variety of local immune responses that correlate with antitumor activity. Nevertheless, very often, this effective treatment with BCG causes several side effects, some of them quite serious.

Our invention proposes an alternative to BCG: the use of *Mycobacterium brumae*, a non-pathogenic mycobacteria with antitumor activity, which works better than the current treatment for non-invasive bladder cancer using BCG.

Mycobacterium brumae grows three times faster and on a cheaper culture media than BCG. *Mycobacterium brumae* has a biosafety level of 1, while BCG has biosafety level 2. Thus, this new treatment could replace BCG, beeing safer, cheaper and easier to produce than BCG.

Only in USA, 75,000 new Bladder Cancer cases are diagnosed every year. Most of cases, when diagnosed are still non-invasive tumors, present only in the mucose or submucose.

An effective treatment does already exist: Immunotherapeutic treatment with BCG, but such treatment is not safe enough. It has been reported to cause important side effects like fever, vomiting, flu symptoms, nausea, difficult urination and even more serious pathogenic consequences: tuberculosis or sepsis. Therefore, safer alternatives are required.

Innovative aspects and applications

> *Mycobacterium brumae* shows an antitumoral activity greater than BCG on low grade bladder cancer cells

> *Mycobacterium brumae* has a similar antitumoral activity than BCG on high grade bladder cancer cells

> *Mycobacterium brumae* treatment trigger enhanced survival rates than BCG treatment on tumor-bearing mice

> *Mycobacterium brumae* has been described as non-pathogenic (level 1) while BCG is level 2, i.e. this new treatment is a promising efficient/safe alternative to BCG.

State of development

Direct antitumoral capacity of *M. brumae* on different tumoral bladder cell cultures has been demonstrated.

The capacity to trigger the activation of the immune system, and the antitumor activity of *Mycobacterium* brumae-activated immune cells has been demonstrated.

Moreover, the in vivo antitumor capacity of *M. brumae* in an orthotopic murine model of bladder cancer has been demonstrated.

Our results show that our therapy is better that BCG therapy

Future development

Scientific results has been shown to physicians and a clinicla trial could be performed in 2015.

IP Rights

PCT Application filed on July 2013

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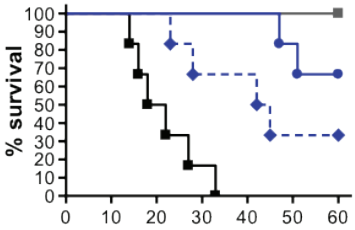
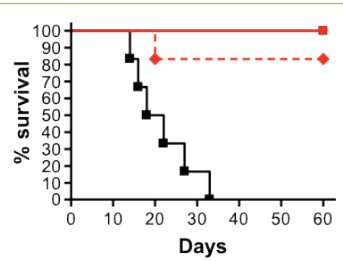
The Invention

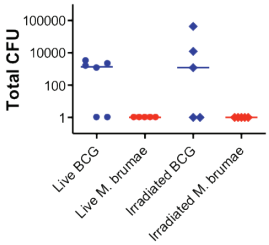
- We propose a promising alternative comprising the use of *Mycobacterium brumae*. That shows to be more effective than BCG on inhibition of tumoral proliferation, specifically on low grade bladder cancer cells (early stages) in vitro.
- *M. brumae* also induces the production of pro-imflammatory cytokines on macrophages and peripheral human blood, and the expression of markers of activation on macrophages.
- M. brumae-activated immune cells show cytotoxic activity agains bladder cancer cells. Gamma-irradiated M. brumae retains its antitumor capacity.
- *M. brumae* prolongs survival in tumor-bearing mice compared to BCG-treated or non-treated mice.
- *M. brumae* is non-pathogenic. *M. brumae* is killed by macrophages, bladder cells and is not recovered from *M. brumae*-treated tumor-bearing mice. Contrary, BCG survive along the time and is recovered from BCG-treated mice, which is reflected in bladder cancer patients since BCG produce illness in some cases.
- *M. brumae* grows three times more rapid than BCG in culture media. Moreover, is considered a biosafety level 1-microorganism, being safer and easy to manipulate in the laboratory than BCG (biosafety level 2).

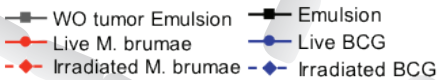
Fig. 1.Survival rates of tumor-bearing mice treated with emulsionated live or irradiated M. brumae and BCG





acteria recovery from spleens of treated tumor-bearing mice





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