ASCO 2021

GUSTAVE ROUSSY CANCER CAMPUS GRAND PARIS

Bergonié UNICANCER NOUVELLE-AQUITAINE

Press release

# Metastatic or recurrent cancer of the uterine cervix
# Encouraging results with second generation immunotherapy

*An early trial presented by the Institut Bergonié and Gustave Roussy at the 2021 ASCO Conference shows that patients with metastatic or recurrent cancer of the cervix may benefit from dual immunotherapy. The new generation agent, Simlukafusp Alfa, a variant of interleukin-2, shows promising signs of efficacy by doubling the response to anti-PD-L1 immunotherapy alone, without causing major adverse effects.*

Oral presentation by
**Prof. Antoine ITALIANO**

**BROADCAST: june 4th 2021 at 15:00**

**READ THE ABSTRACT**
**N°5510**

Can we hope for an immunotherapy revolution in the treatment of cancers of the cervix as has been the case for other cancers, in particular of lung or in melanoma? For six years research has been devoted to discovering whether stimulation of immune defence mechanisms may also be effective in treatment of gynaecological cancers.

With some 3,000 new cases diagnosed each year, ¾ of which are in women aged less than 65, and 1,100 deaths in 2018, *"thanks to early screening for precancerous lesions by cervical smears and now vaccination against the papillomavirus (HPV), tumours of the cervix are not the commonest cancers in France nor the commonest cause of cancer mortality. On a world scale, however, because of the lack of regular gynaecological monitoring, especially in underdeveloped countries, this cancer presents a major public health problem with a high mortality rate,"* declared Professor Antoine Italiano, director of the Gustave Roussy precision medicine programme and head of the early trials unit at the Institut Bergonié (Bordeaux), who is the lead author of the study presented at the ASCO meeting. This study opens up encouraging prospects for the role of novel immunotherapies in the treatment of cervical cancer.

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***¾*** *of which are in women aged less than 65*

When diagnosed early, as a result of surgical treatment, possibly coupled with radiotherapy or chemotherapy, the overall prognosis in the majority of patients is good with a 5-year survival rate of 63%. The risk of relapse, however, is as high as 20-30%, *"and some cancers may be found to be inoperable at the outset,"* emphasised Prof. Italiano. For those women with persistent, recurrent or metastatic cervical cancer, *"the therapeutic options unfortunately remain limited at present, the only possibility being palliative chemotherapy (cisplatin)."*

Faced with this therapeutic impasse and in the light of expectations raised by immunotherapy, several clinical trials have been conducted since 2015 to explore the effects of anti-PD-1/PD-L1 agents in cervical cancer. In 2018 in the United States, on the basis of one of these trials (Keynote 158), the FDA approved a recognised anti-PD-L1 therapeutic agent (pembrolizumab) for the treatment of advanced cervical cancer during or following chemotherapy. In France, the efficacy was not judged to be sufficiently convincing for its use to be authorised.

The early trial presented at ASCO was sponsored by Roche and led by Gustave Roussy and the Institut Bergonié. Its objective was to assess the safety and efficacy of a different strategy: the combination of an anti-PD-L1 (atezolizumab) with a novel second generation immunotherapeutic agent - Simlukafusp Alfa, an interleukin-2 variant (IL-2v), the safety of which had already been tested when used as monotherapy. Its mode of action complements that of "conventional" immunotherapy with a similar goal: stimulation of the body's natural immune defence mechanisms. Atezolizumab targets the PD-1 protein, which when expressed in tumour cells prevents lymphocytes from recognising that they are inimical. *"Once the capacity to recognise cancer cells has been restored, they require a boost: Simlukafusp Alfa stimulates the NK (natural killer) lymphocytes so that their innate capacity to kill tumour cells is restored,"* summarised Prof. Italiano.

The 47 patients recruited for this multicentric phase 1B trial had relapsed or metastatic cervical cancer. Their median age was 53 years. Over a third of them had already received more than one line of standard treatment (surgery, radiotherapy or chemotherapy) and were in a situation of therapeutic failure with life expectancy being less than one year. Tumour cells expressed the PD-L1 protein in 51% of the patients. All of them, however, received the same medication with no additional therapy: intravenous infusion of atezolizumab (1,200 mg) and simlukafusp (10 mg), at three-weekly intervals. *"The treatment was continued for as long as it remained effective up to a total period of 18 months,"* specified the oncologist. *"The measures of efficacy were promising with a slight advantage in those patients whose tumour expressed PD-L1,"* explained Prof. Italiano. *"For a little over a quarter of the patients (27%) there was an objective response to treatment with a reduction of more than 30% in tumour size. Approximately ¾ of the patients were classed as having responded when those in whom tumour size was stabilised were also included."* The response to treatment appeared to be durable: a median value of 13.3 months.

*"For 27% of the patients there was an objective response to treatment with a reduction of more than 30% in tumour size."*

Trials of anti-PD-L1 administered as monotherapy have never shown this degree of efficacy. *"The level of response with atezolizumab alone would not exceed 10%,"* emphasised Prof. Italiano.

Adverse effects were seen in all of the patients (63.8% grade 3 and 29.8% grade 4). *"With immunotherapy the most frequently observed reaction is fever during the period of infusion, which is easily managed by administering paracetamol,"* stated Prof. Italiano.

These initial results are encouraging and argue for continuing research with these novel agents and for combining them with first generation immunotherapeutic agents to increase the chances of success in those patients for whom the therapeutic options are currently limited.

## ABOUT

**Classed as the leading European Cancer Centre and the fifth on the world stage,** Gustave Roussy is a centre with comprehensive expertise and is devoted entirely to patients suffering with cancer. It is a source of diagnostic and therapeutic advances. It caters for almost 50,000 patients per year and its approach is one that integrates research, patient care and teaching.

It is specialised in the treatment of rare cancers and complex tumours and it treats all cancers in patients of any age. Its care is personalised and combines the most advanced medical methods with an appreciation of the patient's human requirements. In addition to the quality of treatment offered, the physical, psychological and social aspects of the patient's life are respected.

3,200 health professionals work on its two campuses: Villejuif and Chevilly-Larue. Gustave Roussy brings together the skills which are essential for the highest quality research in oncology: a quarter of patients treated are included in clinical trials.

For further information: **www.gustaveroussy.fr/en**

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