GUSTAVE ROUSSY IN ASCO 2019

Press release / Oral session / Chicago, 4th June 2019

MELANOMA

The advantages of targeted dual therapy confirmed at five years

Treatment of metastatic melanoma patients with *BRAF* V600 mutation using a combination of dabrafenib and trametinib (two anti-cancer agents which act on an intracellular signalling pathway specifically involved in the cancer process) prolongs progression-free survival and improves overall survival for many patients, according to the latest results, at 5 years, that confirm the value of this targeted dual therapy. Presented at the ASCO meeting and published simultaneously in the *New England Journal of Medicine (NEJM)*, these are the findings of a combined analysis of data from two studies, COMBI-d and COMBI-v, conducted, in particular, by Professor Caroline Robert, head of the Dermatology Department at Gustave Roussy.

ORAL SESSION
Tuesday 4th June
11:57 AM – 12:09 PM
(Chicago time)
Room S406

READ THE ABSTRACT
N° 9507

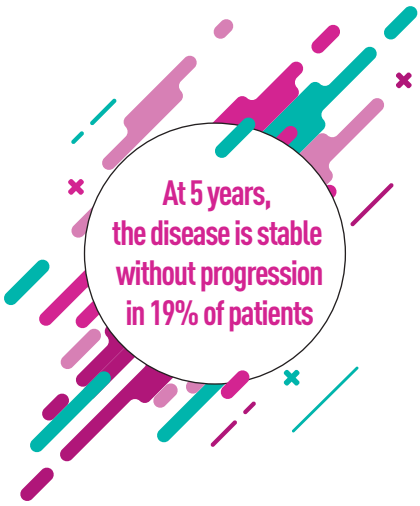
The COMBI-d and COMBI-v trials both evaluated the safety and efficacy of the combination of dabrafenib and trametinib, two protein kinase inhibitors which target RAF and MEK respectively. This combined targeted therapy was compared with monotherapy in patients with metastatic melanoma with a BRAF V600E/K mutation. The first results of combined analysis of both trials after 3 years were published in 2017. They showed that the disease had not progressed in 23% of the patients and that 44% were still alive. In this new study, presented at ASCO and published simultaneously in the NEJM, these improvements are confirmed at 4 and 5 years with the disease stabilised in 21 and 19% of patients respectively and with overall survival figures reaching 37 and 34%.

"Presentation of the results of this study at the ASCO Conference and joint publication in the NEJM are very gratifying as they show the long-term benefits of targeted therapy at a time when this approach to cancer therapy is being neglected somewhat in favour of immunotherapy," **commented Professor Robert.**

The pooled COMBI study examined data from 563 patients with metastatic melanoma carrying BRAF V600E/K mutation. These patients were participants in the COMBI-d (211) or COMBI-v (352) phase 3 trials. They were treatment-naive at the time of inclusion and received two doses per day of 150 mg of dabrafenib combined with a single daily dose of 2 mg of trametinib.

At 4 and 5 years, the progression-free and overall disease survival rates seemed to have reached a plateau, suggesting stabilisation of treatment efficacy. The authors did, however, observe some disparities between patients according to the number of metastases and levels of serum LDH (Lactate dehydrogenase, an enzyme, elevation of which is a sign of aggressive melanoma).

- Thus, 25% of the patients whose disease had not progressed had normal levels of LDH compared with only 8% of those whose levels were high; the overall survival figure was also considerably higher at 43% vs 16% ;
- And in patients who had both a normal LDH and less than 3 metastatic deposits, these values rose to 31% and 55% respectively.



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Work will continue to define the sub-groups of patients who are most likely to benefit from this targeted dual therapy. It seems at present that a complete response to targeted dual therapy constitutes an early reliable predictive factor for prolonged progression-free and overall survival.

Of the 300 patients who received another agent on cessation of targeted dual therapy, the great majority were treated with immunotherapy (51% received an antibody inhibiting the T-lymphocyte CTLA-4 regulatory point and 34 % an anti-PD1). ***"Clinical trials evaluating the safety and efficacy of treatment combining a targeted therapy and an anti-PD1 are ongoing, in order to examine the effects of immunotherapy with switches of targeted therapy,"*** **stated Professor Robert.** ***"The results ought to be published in less than a year from now," she said.***

Almost all of the participants reported adverse effects (98%) but all of these were known and expected: fever, skin rash, diarrhoea, etc., different from those seen with anti-PD1 immunotherapy. These effects led 18% of the patients to stop their medication.

In overall terms, "***An objective response was obtained in 68% of the treated patients,"*** **reported Professor Robert,** ***"And almost 20% of patients had a complete response with no metastasis remaining visible after only a few months of treatment with this dual therapy."***

These good results should not, however, mask mortality figures which remain high: 62% at the time when the data were analysed. ***"Even though good progress has been made in the last few years, there are still many deaths by 5 years,"*** **cautioned Professor Robert.**

ABOUT MELANOMA

Melanoma is a skin cancer which arises from the skin cells that produce melanin. About 20% of melanomas result from malignant transformation of a beauty spot . However, in the great majority of cases (80%), the melanoma appears spontaneously, having developed from healthy cells[1].

In 2012, the number of melanoma cases in France was estimated to be 11,176, corresponding to between 2 and 3% of all cancers[1]. The incidence (annual number of new cases) has been increasing by about 10% per year for some 50 years. The mean age at diagnosis is 561.

Although it is far from being the commonest, melanoma is the most serious skin cancer. In common with many cancers, its prognosis is improved by early diagnosis. However, about ¼ of melanomas in France are diagnosed at an advanced stage (stage 3 or metastatic). The 5-year survival rate was 88% for localised disease but only 18% when metastases were present.

[1] Skin melanoma: key points. National Cancer Institute https://www.e-cancer.fr/Patients-et-proches/Les-cancers/Melanome-de-la-peau/Points-cles
[2] Skin melanoma. Guide HAS, january 2012 https://www.has-sante.fr/portail/upload/docs/application/pdf/2012-03/ald_30_guide_melanome_web.pdf

LISTEN TO Pr. CAROLINE ROBERT'S EXPLANATIONS

ALMOST 20% of patients no longer have visible metastases a few months after starting treatment.

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/ Regarding Gustave Roussy

Gustave Roussy, the leading cancer center in Europe, is a comprehensive hub of expertise in oncology, entirely devoted to patients. It employs 3,100 professional staff engaged in patient care, research and teaching.

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