GUSTAVE ROUSSY
CANCER CAMPUS
GRAND PARIS

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Press release

CHILDHOOD CANCERS:
Early promising results of a dual therapy in treatment of some low grade gliomas

Oral dabrafenib-trametinib combination therapy is already recognised treatment for certain melanomas and lung cancers. This might also help in children with low grade gliomas carrying the BRAF V600 mutation. Data from the phase I/IIa multicentre study presented at ASCO show that this combination of two protein kinase inhibitors reduces the size of lesions in the majority of patients and that the side effect profile is satisfactory.

By targeting two enzymes (BRAF and MEK) involved in signalling pathways in certain cancer cells, dabrafenib and trametinib inhibit tumour proliferation. From 2013, combining these two targeted therapies has been known to be effective in some cancers. The combination of these two oral agents is indicated at present only for some adult cancers: non-small cell lung cancers and inoperable or metastatic melanoma, and as post-resection adjuvant treatment of stage III melanoma, when genetic analysis of these tumours shows the presence of a BRAF V600 mutation. This is the case in 40% of melanomas. ***"10 to 20% of low grade gliomas in children also carry this mutation,"*** **pointed out Dr. Birgit Geoerger,** onco-paediatrician, head of the Laboratory for Development of Novel Therapies for Paediatric Tumours at Gustave Roussy and principal investigator in the trial presented at an oral virtual session at ASCO 2020. The trial evaluated the safety and efficacy of the dabrafenib-trametinib combination in children with this cancer type.

Low grade gliomas are the commonest childhood cerebral tumours. Although low grade gliomas grow slowly, they still pose a problem. They are not always entirely operable. Complementary radiotherapy to destroy the remaining malignant cells following surgery ***"is often omitted because of significant effects of cerebral irradiation on cognitive function,"*** **explained Dr. Geoerger.** Standard treatment is therefore based on carboplatin and vincristine chemotherapy for about one year. As soon as promising dabrafenib results appeared for tumours carrying the BRAF mutation, ***"we started to treat children with this histological sub-group. The findings were encouraging,"*** **explained Dr. Geoerger.** ***"All the studies conducted using the dabrafenib-trametinib combination in a number of adult cancers showed that although the response was not necessarily better than with dabrafenib alone, the combination did prevent escape from treatment more effectively."***

Oral presentation
by **Dr. Birgit Geoerger**

READ THE ABSTRACT
N° 10506

EXPLANATIONS IN VIDEO

10 to 20% of low grade gliomas in children carry the BRAF V600 mutation.

Starting in 2015, 36 patients aged less than 18 with low grade gliomas carrying the BRAF V600 mutation were recruited from 16 Cancer Centres in 5 countries to the phase I/II trial to assess for the first time in paediatric practice the safety and efficacy of this dual therapy. The mean age was 10 and only a single patient was less than one year-old. Patients had been diagnosed 40 months (median value) earlier and had already received chemotherapy. All were given the oral combined targeted therapy (in tablet or liquid form depending to their age) in doses previously determined by the research group: dosage of 5.25 mg/kg/day or 4.5 mg/kg/day of dabrafenib divided into two equal doses per day for children aged less or more than 12 respectively. Trametinib dosage was 0.032 mg/kg/day as a single dose for those under six years of age and 0.025 mg/kg/day for the older children. The cut-off for the data analysis of the trial was on 16th August 2019. The data presented at ASCO demonstrate a clinical effect of the targeted dual therapy with an 89% measure of disease control (stability or regression of lesions seen on imaging and defined by an independent review). The median duration of treatment administered was 14 months. 26 children remain on treatment ***"and some have now been on it for more than 40 months,"*** **emphasised Dr. Geoerger.** The main adverse effects seen – fever and dermatological features (dry skin and rash) – were predominantly of low grade: ***"surprisingly these agents prove to be better tolerated in combination than when administered singly,"*** **observed Dr Geoerger,** ***"and side effects were easily controlled."***

The research group is now going to extend its work by comparing the benefits of the dabrafenib-trametinib combination with those of conventional chemotherapy over one year in patients with newly diagnosed low grade glioma.

"The dabrafenib-trametinib combination limits tumour escape and the side effect profile is better than that seen with monotherapy.

The disease control value is 89%.

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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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