



Fondation du Centre  
Pluridisciplinaire d'Oncologie

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CHUV BH 06 - Rue du Bugnon 46 - 1011 Lausanne

### ZOOM MO25653

<b>Indication</b>	Metastatic melanoma with brain metastases, harboring the BRAF V600 mutation
<b>Title</b>	An open-label, pilot study of RO5185426 in previously treated metastatic melanoma patients with brain metastases
<b>Protocol ID</b>	<b>MO25653</b>
<b>Phase</b>	<b>Phase II</b>
<b>Sponsor</b>	Hoffmann-La Roche Ltd
<b>Local Principal Investigator</b>	Pr Olivier Michielin
<b>Primary Objective</b>	To evaluate the safety and tolerability of RO5185426 in patients with metastatic melanoma with brain metastases (Stage IV; AJCC) harboring the BRAF V600 mutation.
<b>Inclusion/exclusion criteria</b>	<b>Inclusion Criteria include the following :</b> <ul style="list-style-type: none"><li>○ Male or female patients <math>\geq 18</math> years of age</li><li>○ Patients with histologically confirmed metastatic melanoma (Stage IV, AJCC) with documented BRAF V600 mutation as determined by the cobas® BRAF V600 Mutation Test prior to administration of RO5185426</li><li>○ Presence of brain metastases where surgical resection is not a treatment option</li><li>○ Patients must have failed at least one previous treatment for brain metastases, requiring treatment with corticosteroids for symptom control, and are without satisfactory treatment options</li><li>○ Stable or decreasing corticosteroids dose within 1 week prior to study entry.</li><li>○ Patients with either measurable or non-measurable disease (RECIST Version 1.1).</li><li>○ ECOG PS of 0-2</li><li>○ Patients must have recovered from all side effects of their most recent systemic or local treatment for metastatic melanoma</li><li>○ Adequate hematologic, renal and liver function as defined by the following laboratory values performed within 7 days prior to initiation of dosing:<ul style="list-style-type: none"><li>• ANC <math>\geq 1.5 \times 10^9/L</math></li><li>• Platelet count <math>\geq 100 \times 10^9/L</math></li><li>• Hemoglobin <math>\geq 9 \text{ g/dL}</math></li><li>• Serum creatinine <math>\leq 1.5</math> times ULN or CrCl <math>&gt; 50 \text{ mL/hr}</math> by Cockcroft–Gault formula</li></ul></li></ul>

- AST and ALT  $\leq$  2.5 times ULN ( $\leq$  5 times ULN if considered due to tumor)
- Serum Bilirubin  $\leq$  1.5 times ULN
- Alkaline phosphatase  $\leq$  2.5 times ULN ( $\leq$  5 times ULN if considered due to tumor)
- Negative serum pregnancy test within 7 days prior to commencement of dosing in premenopausal women. Women of non-childbearing potential may be included if they are either surgically sterile or have been postmenopausal for 1 year
- Fertile men and women must use an effective method of contraception during treatment and for at least 6 months after completion of treatment as directed by their physician.
- Absence of any psychological, familial, sociological or geographical condition potentially hampering compliance with the study protocol and follow-up schedule; those conditions should be discussed with the patient before trial entry
- Signed informed consent must be obtained prior to performing any study-related procedures (including tumor testing for the V600 BRAF mutation)

**Exclusion Criteria include the following:**

- Increasing corticosteroid dose during the 7 days prior to study entry
- Patients with a previous malignancy within the past 2 years are excluded except for patients with basal or SCC of the skin or carcinoma in-situ of the cervix. Isolated elevation in prostate-specific antigen (PSA) in absence of radiographic evidence of metastatic prostate cancer is allowed
- Concurrent administration of any anticancer therapies (e.g. chemotherapy, other targeted therapy, experimental drug, etc) other than those administered in this study
- Treatment with any cytotoxic and/or investigational cytotoxic drug or targeted therapy  $\leq$  2 weeks prior to Day 1 of study
- Pregnant or lactating women
- Refractory nausea and vomiting, malabsorption, external biliary shunt, or significant bowel resection that would preclude adequate absorption. Patients must be able to swallow tablets
- Any of the following within the 6 months prior to study drug administration: myocardial infarction, severe/unstable angina, symptomatic congestive heart failure, cerebrovascular accident or transient ischemic attack, pulmonary embolism, hypertension not adequately controlled by current medications
- History of or presence of clinically significant ventricular or atrial dysrhythmia  $\geq$  Grade 2 (NCI CTCAE Version 4.0)
- Corrected QTc interval  $\geq$  450 msec at baseline
- Uncontrolled medical illness such as infection requiring treatment with IV antibiotics
- Other severe, acute or chronic medical or psychiatric condition

	<p>or laboratory abnormality that may increase the risk associated with study participation or study drug administration, or may interfere with the interpretation of study results, which in the judgment of the investigator would make the patient inappropriate for entry into this study</p> <ul style="list-style-type: none"><li>○ Unwillingness to practise effective birth control</li><li>○ Inability to comply with other requirements of the protocol</li></ul>
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