Supplementary Table 1. Eligibility/ineligibility criteria and inclusion/exclusion criteria.

Eligibility Criteria:

1. Patients must be at least 18 years of age.
2. Patients must have histologically confirmed diagnosis of Stage IV metastatic melanoma positive for BRAF V600E mutation by a CLIA approved assay.
3. Patients must have a ECOG performance status of 0 or 1 (EOCG, Eastern Cooperative Oncology Group; Oken, M.M. et al. Am J Clin Oncol 5:649-655, 1982).
4. Patients must have the following hematologic, renal and liver function: absolute neutrophil count > 1500/mm3, platelets > 100,000/mm^3, creatinine ≤ 2 times the upper limits of normal (ULN), albumin > 2g/dL, total bilirubin ≤ 1.5 mg/dl, ALT and AST ≥3 times above the upper limits of the institutional norm.
5. Patients must be able to provide written informed consent.
6. Negative serum pregnancy test within 7 days prior to commencement of dosing in premenopausal women. Women of non-childbearing potential may be included without serum pregnancy test 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. Effective methods of contraception are defined as those which result in a low failure rate (i.e., less than 1% per year) when used consistently and correctly (for example implants, injectables, combined oral contraception or intra-uterine devices). At the discretion of the Investigator, acceptable methods of contraception may include total abstinence in cases where the lifestyle of the patient ensures compliance. (Periodic abstinence [e.g., calendar, ovulation, symptothermal, postovulation methods] and withdrawal are not acceptable methods of contraception.)
7. Patients with treated brain metastases that have been stable for 1 month are eligible; patients must be off steroids for 1 week prior to starting study treatment.
8. Any number and type of prior anticancer therapies except BRAF or MEK inhibitors.
9. Patients must have discontinued active immunotherapy (IL-2, interferon, CTLA-4, etc.) or chemotherapy at least 4 weeks prior to entering the study and oral targeted therapy at least 2 weeks prior to entering the study and have recovered from adverse events due to those agents. Patients must not receive any other investigational anticancer therapy during the period on study or the four weeks prior to entry, with the exception of vaccines.
10. Patient much have measurable disease as defined by the Response Evaluation Criteria in Solid Tumors (RECIST); guideline (version 1.1) (Eur J Cancer. 2009 Jan;45(2):228-247).

Ineligibility Criteria

1. Patients with serious concurrent infection or medical illness, including psychiatric disorders, which would jeopardize the ability of the patient to receive the treatment outlined in this protocol with reasonable safety.
2. Patients who are pregnant or breast-feeding.
3. Patients receiving concurrent therapy for their tumor (i.e. chemotherapeutics or investigational agents).
4. Patients with leptomeningeal disease
5. Patients who are known to be experiencing an objective partial response to immunotherapy at the time of study enrollment are ineligible.
6. Patients with a concurrent or prior malignancy within the last 2 years, unless they are patients with curatively treated carcinoma-in-situ at any site, or basal cell carcinoma or squamous cell carcinoma of the skin. Patients with treated prostate cancer or breast cancer for which

no concurrent therapy is indicated are eligible for this study. Patients who have been free of disease (any prior malignancy) for five years are eligible for this study.

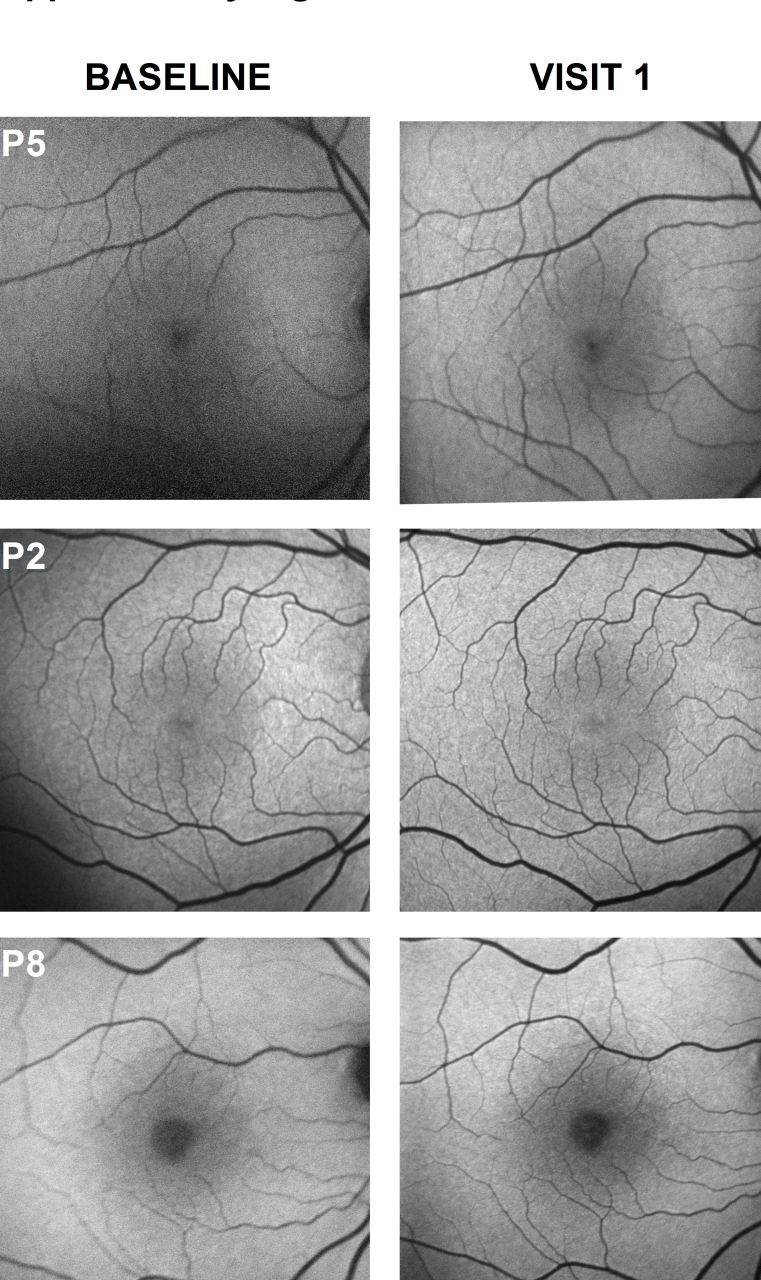
7. History of interstitial lung disease or pneumonitis
8. Due to risk of disease exacerbation patients with psoriasis are ineligible unless the disease is well controlled and they are under the care of a specialist for the disorder who agrees to monitor the patient for exacerbations.
9. Have a known immediate or delayed hypersensitivity reaction or idiosyncrasy to drugs chemically related to study drug, or excipients or to dimethyl sulfoxide (DMSO).
10. Patients receiving cytochrome P450 enzyme-inducing anticonvulsant drugs (EIADs) (i.e. phenytoin, carbamazepine, Phenobarbital, primidone or oxcarbazepine) are ineligible.
11. Patients with previously documented macular degeneration,diabetic retinopathy, or retinal vein occlusions, uveitis, central serous retinopathy, pattern dystrophy of the macula, and patients at risk for angle closure glaucoma from pupillary dilation are ineligible.
12. Patients with prior exposure to BRAF or MEK inhibitors are not eligible.
13. History or evidence of increased cardiovascular risk including any of the following:
    - Left ventricular ejection fraction (LVEF) < institutional lower limit of normal.
    - A QT interval corrected for heart rate using the Bazett's formula ≥480 msec.
    - Current clinically significant uncontrolled arrhythmias.
    - Exception: Subjects with controlled atrial fibrillation for >30 days prior to randomization are eligible.
    - History of acute coronary syndromes (including myocardial infarction and unstable angina), coronary angioplasty, or stenting within 6 months prior to randomization.
    - Current ≥ Class II congestive heart failure as defined by New York Heart Association [http://www.heart.org/HEARTORG/Conditions/HeartFailure/AboutHeartFailure/Classes-of-Heart-Failure_UCM_306328_Article.jsp.]

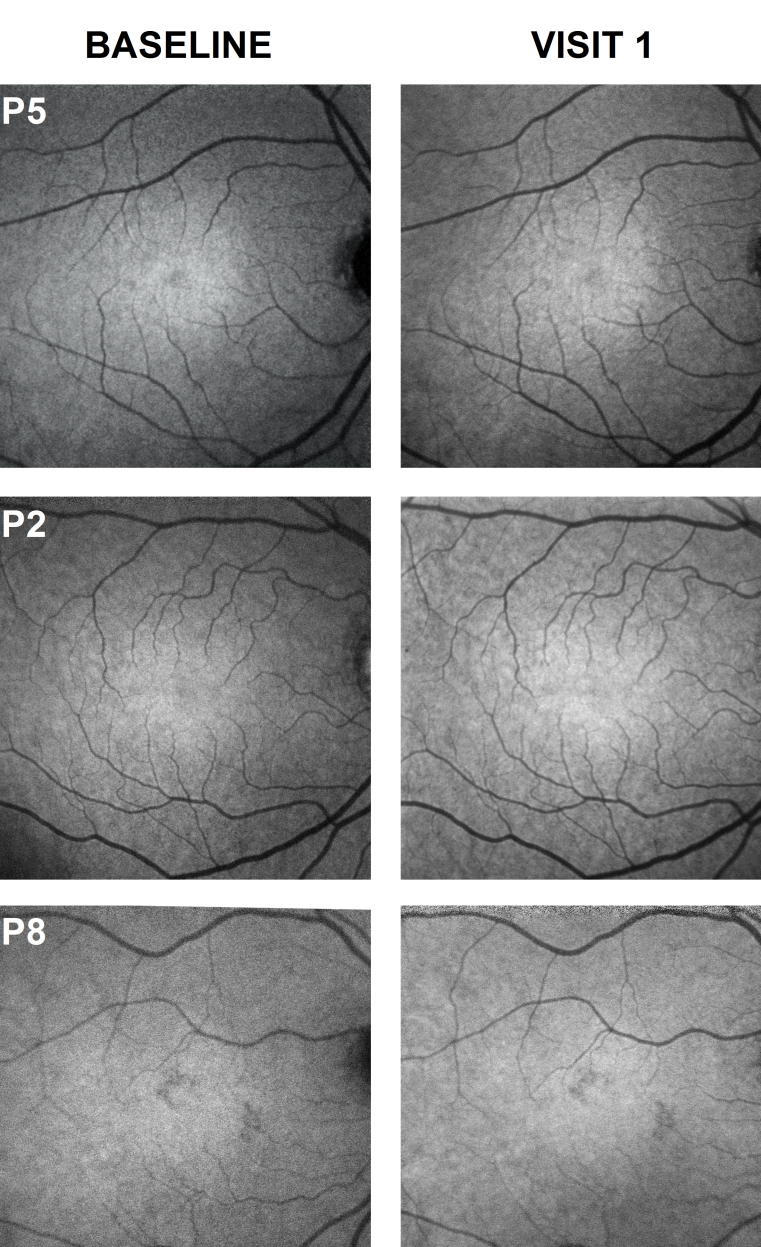
Inclusion Criteria:

1. ≥ 18 years of age.
2. Histologically confirmed Stage IV metastatic melanoma positive for BRAF V600E mutation by a CLIA approved assay.
3. ECOG performance status of 0 or 1
4. Adequate renal, liver, and hematological function
5. Able to provide written informed consent.
6. Treated brain metastases that have been stable for 1 month are eligible; patients must be off steroids for 1 week prior to starting study treatment.
7. Any number and type of prior anticancer therapies except BRAF or MEK inhibitors.

Exclusion Criteria:

1. Diagnoses of HIV, porphyria, uncontrolled psoriasis, and existing retinopathy, concurrent malignancies within the last 2 years except for prostate cancer and breast cancer for which no concurrent therapy is indicated.
2. History of use of P450-inducing anticonvulsant drugs.


BASELINE
VISIT 1
P5
P2
P8


BASELINE
VISIT 1
P5
P2
P8