Patients were randomized 1:1:1 to receive either encorafenib 450 mg once daily + binimetinib 45 mg twice daily (COMBO450), encorafenib 300 mg once daily (ENCO300), or vemurafenib 960 mg twice daily (VEM 960 mg BID). In an update of the study, median overall survival was 33.6 months with encorafenib plus binimetinib compared with 16.9 months with vemurafenib.\(^\text{10}\) Each of the established combinations (dabrafenib plus trametinib and vemurafenib plus cobimetinib) has a distinct safety profile with unique toxicities that impact overall survival.3,4 Photosensitivity has been commonly seen in patients treated with vemurafenib plus cobimetinib.\(^\text{3,4}\) In the COMBO450 group, 24% of patients experienced a maximum grade of grade 1, 6% of grade 2, 10% of grade 3, and 2% of grade 4. No serious unexpected AEs were observed. In patients treated with COBIM450, photosensitivity was common and was mainly associated with disease progression or underlying skin conditions.10 Series of vitreous hemorrhages and serous retinopathy were mainly asymptomatic (grade 1) or of low severity and grade 2.\(^\text{2,5}\) Vomiting occurred in 30% of patients in the COMBO450 group, in 27% in the ENCO300 group, and in 19% of patients in the VEM group (8% compared with the ENCO300 (2%) and VEM groups (1%).\(^\text{2,5}\)

### References

1. VRepresenting the 15% of the study sample that was used for the AESIs reported in this study.\(^\text{2,5}\)
2. The cutoff date for these analyses was May 19, 2016.\(^\text{2,5}\)
3. Safety was assessed in all patients who received at least one dose of study drug and had a least one post-baseline assessment of an AESI.\(^\text{2,5}\)
4. The AESIs are defined based on the National Cancer Institute’s Common Terminology Criteria for Adverse Events (CTCAE), version 4.0.\(^\text{2,5}\)
5. The use of the term “serious” is consistent with the definition in the CTCAE.\(^\text{2,5}\)
6. The use of the term “adverse event” is consistent with the definition in the CTCAE.\(^\text{2,5}\)
7. Four patients experienced a maximum grade of grade 2 photosensitivity in the ENCO300 group (2% compared with the VEM group [1%]).\(^\text{2,5}\)
8. VEM = vemurafenib 960 mg twice daily; COMBO450 = encorafenib 450 mg once daily plus binimetinib 45 mg twice daily; CuSCC = cutaneous squamous cell carcinoma.\(^\text{2,5}\)
9. Unless otherwise stated, all patients received study drug for at least one cycle of 28 days.\(^\text{2,5}\)
10. Photosensitivity has been commonly seen in patients treated with vemurafenib plus cobimetinib.\(^\text{3,4}\) Series of vitreous hemorrhages and serous retinopathy were mainly asymptomatic (grade 1) or of low severity and grade 2.\(^\text{2,5}\) Vomiting occurred in 30% of patients in the COMBO450 group, in 27% in the ENCO300 group, and in 19% of patients in the VEM group (8% compared with the ENCO300 (2%) and VEM groups (1%).\(^\text{2,5}\)

### CONCLUSIONS

- Common BRAF/MEK inhibitors are generally manageable, and this study associated with treatment discontinuation.
- No serious unexpected AEs were observed.
- In patients treated with COBIM450, photosensitivity was common, and was mainly associated with disease progression or underlying skin conditions.
- Photosensitivity was common, and it was generally reversible and did not require discontinuation of treatment.
- This analysis of AESIs suggests that COBIM450 is generally well-tolerated in patients with BRAFV600E-mutant melanoma.