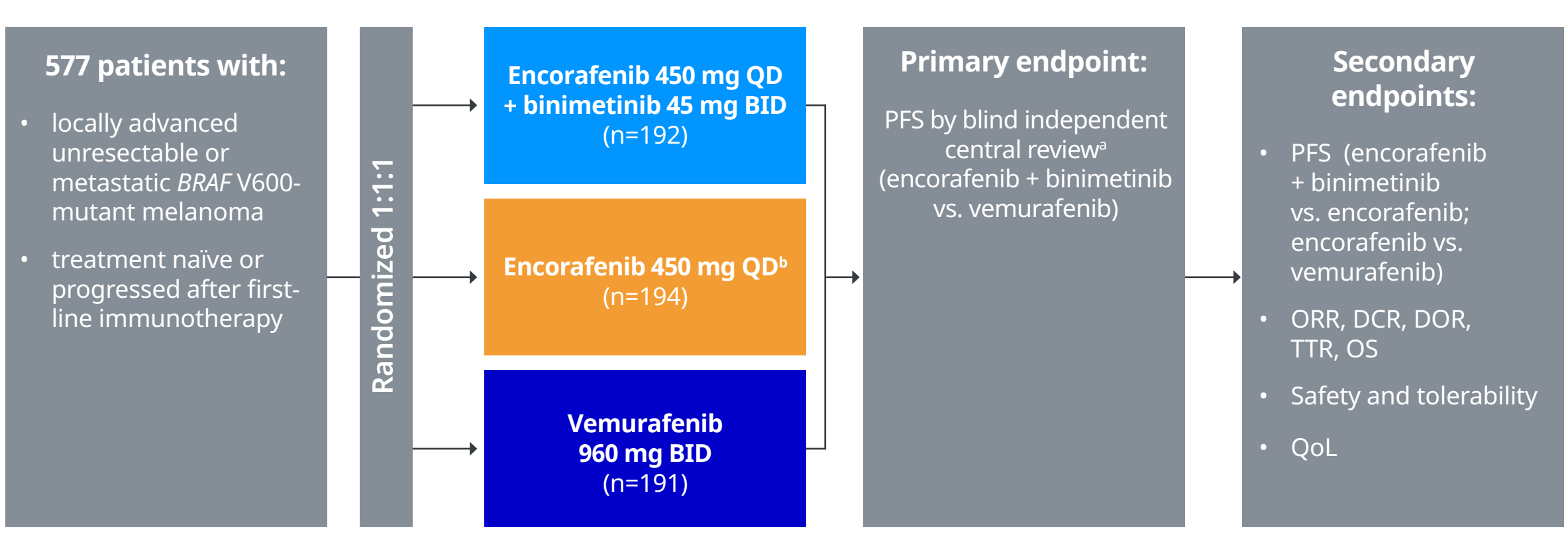
7-year update on the COLUMBUS Study

What is the COLUMBUS Study?

The COLUMBUS study (NCT01909453) is a phase III, randomized, multicenter, open-label, active-controlled study, assessing the safety and efficacy of encorafenib plus binimetinib vs. vemurafenib or encorafenib alone in patients with unresectable or metastatic *BRAF* V600E/K-mutant melanoma.[1,2]



Stratified by AJCC stage, ECOG PS, and *BRAF* mutation status/prior first-line immunotherapy.[c]

COLUMBUS Study Design

Figure adapted from Schadendorf D, et al 2024 and Dummer R, et al 2018[1,2]

[a]Data from tumour assessments for primary and secondary endpoints were assessed centrally by blinded independent central review (BICR) and local review according to guidelines based on RECIST version 1.1.[2,3]

[b]Please note, the results for the encorafenib alone arm are not reported as this indication is currently not approved.[4]

[c]Prior first-line immunotherapy replaced BRAF mutation status as a stratification factor after protocol amendment 2.[1]

What is the background to the COLUMBUS study?

50%

BRAF V600E/K mutations occur in approximately 50% of patients with melanoma.[3,5]

Dual *BRAF/MEK* inhibitor regimens are a treatment option for patients with *BRAF* V600E/K-mutant metastatic melanoma.[3,5,6]

In the primary analysis of the COLOMBUS study, encorafenib + binimetinib was associated with improved PFS and OS vs. vemurafenib alone in patients with unresectable or metastatic *BRAF* V600-mutant melanoma.[2]

What was the aim of the 7-year analysis of the COLUMBUS study?

93 months

In this post-hoc analysis of COLUMBUS, efficacy and safety were assessed after a minimum follow-up of 93 months.[1a]

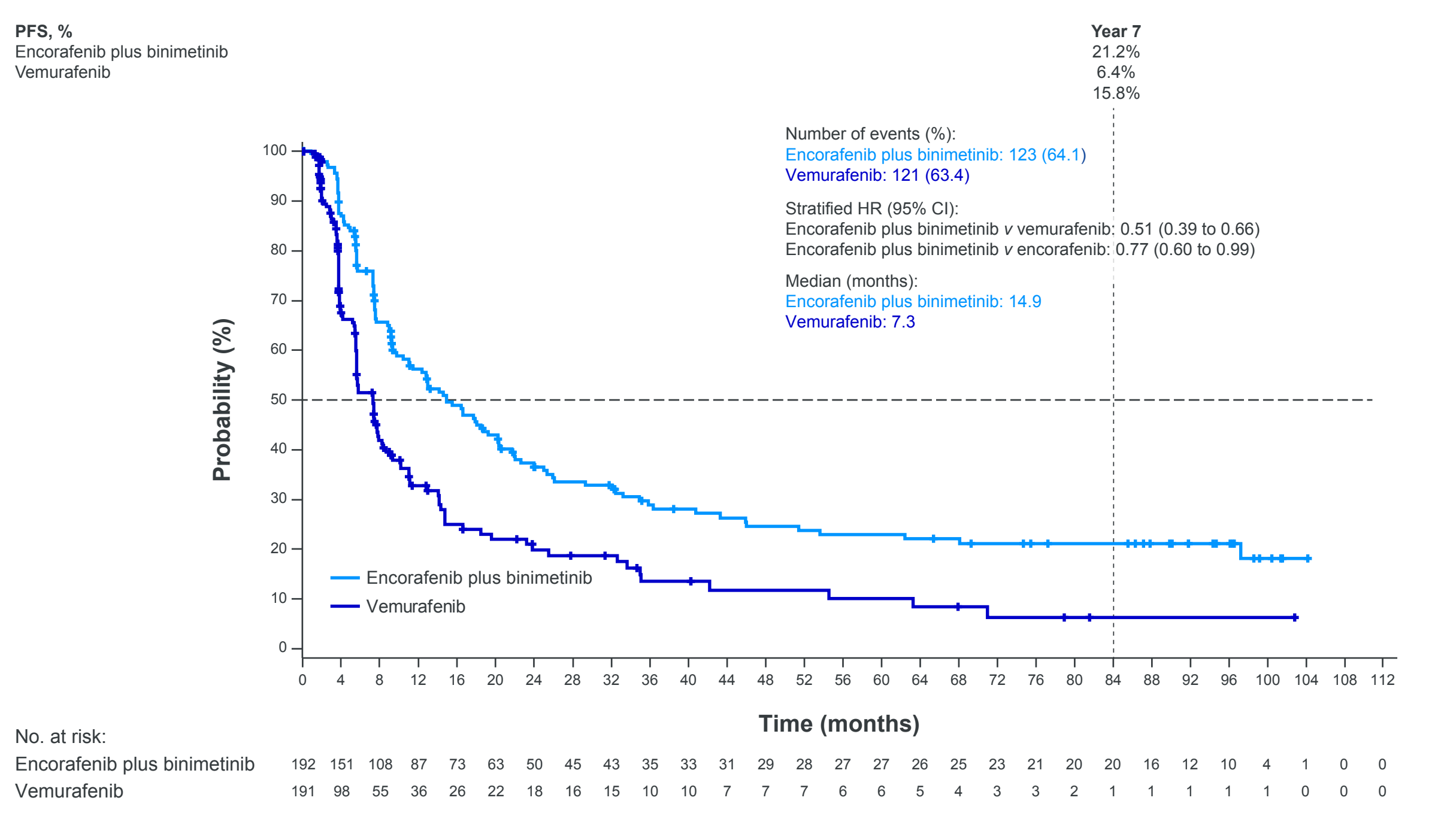
This is the longest follow-up from a phase III trial of *BRAF*/MEK inhibitor combination in *BRAF* V600E/K-mutant metastatic melanoma.[1]

[a]Please note, the results for the encorafenib alone arm are not reported as this indication is currently not approved.[4]

What do the 7-year results tell us about efficacy?

Progression-Free Survival

At the 7-year post-hoc analysis, the PFS rates were 21.2% in the encorafenib + binimetinib arm (95% CI: 14.7%, 28.4%) and 6.4% in the vemurafenib alone arm (95% CI: 2.1%, 14.0%).[1]

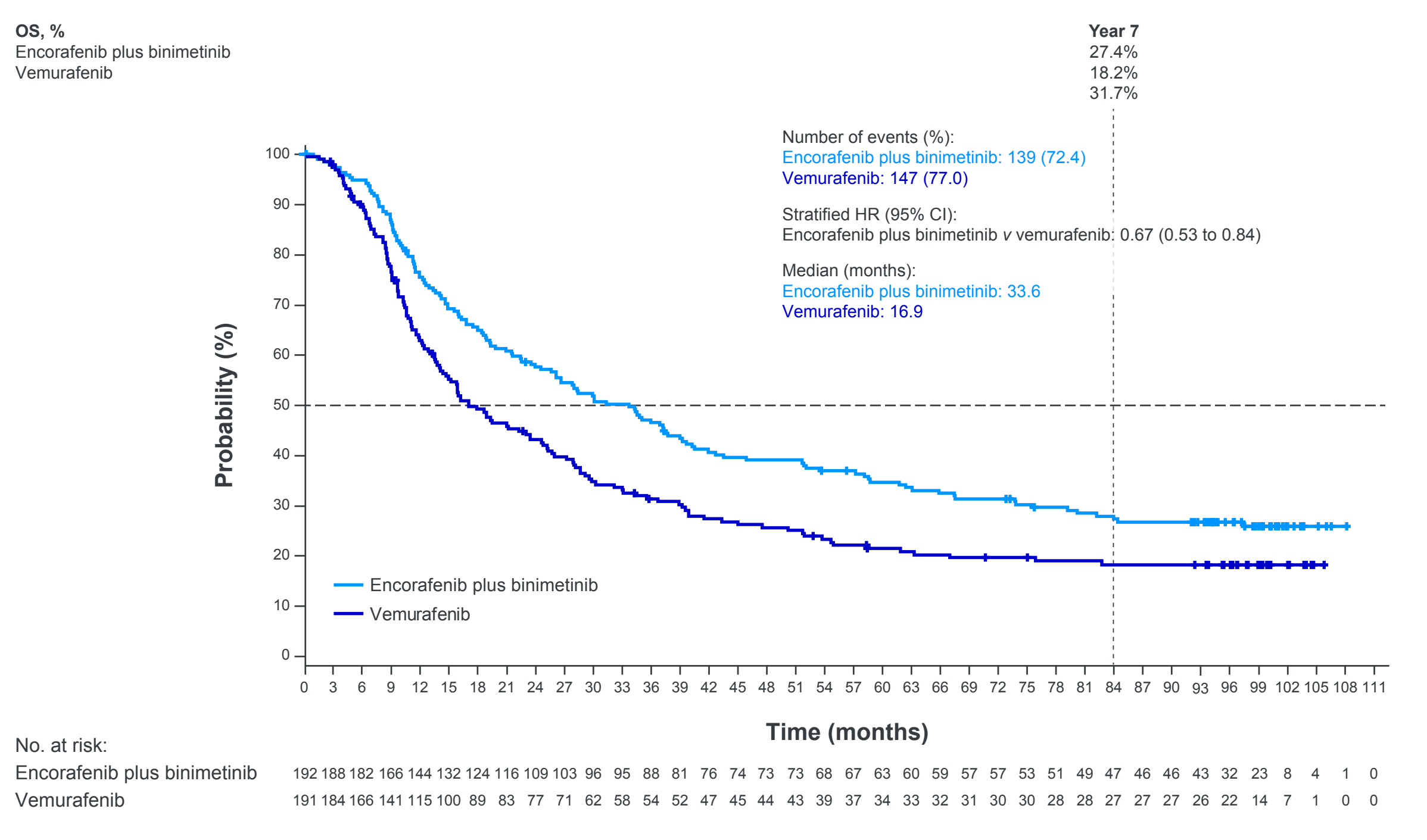


Progression-Free Survival

Figure adapted from Schadendorf D, et al 2024[1]

Overall Survival

The 7-year post-hoc OS rates were 27.4% (95% CI: 21.2%, 33.9%) in patients who received encorafenib + binimetinib, and 18.2% (95% CI: 12.8%, 24.3%) patients who received vemurafenib.[1]

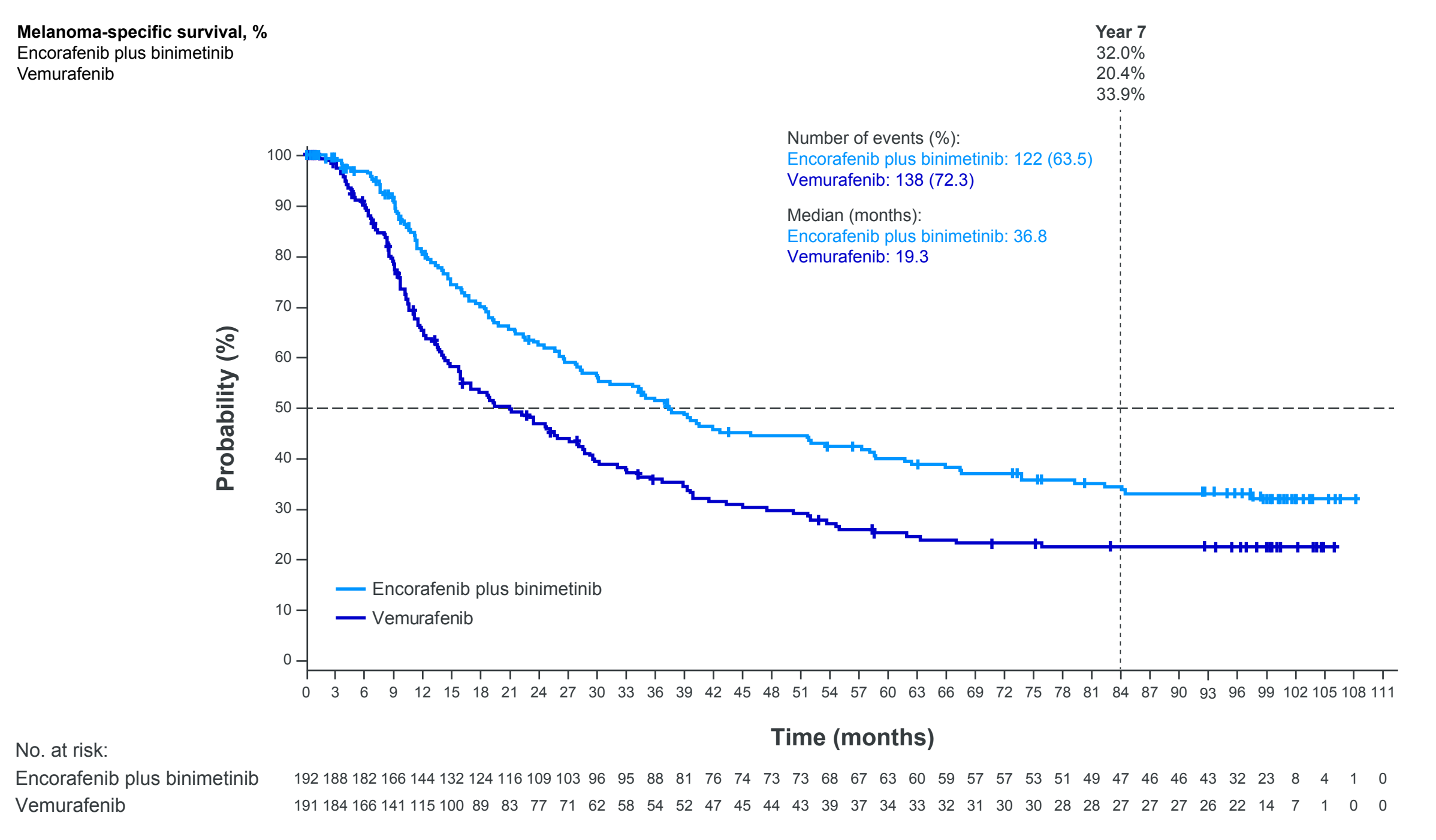


Overall Survival

Figure adapted from Schadendorf D, et al 2024[1]

Melanoma-Specific Survival

Median melanoma-specific survival was 36.8 months in patients who received encorafenib + binimetinib (95% CI: 27.7-51.5) and 19.3 months with vemurafenib alone (95% CI: 14.8-25.9).[1]



Overall Survival

Figure adapted from Schadendorf D, et al 2024[1]

[a]Patients whose primary reason for death is 'study indication' or 'other' with melanoma or disease progression as the specified reason are considered as having an event. Patients who died of all other reasons are censored at the death date, while patients who are alive are censored at the last contact date.[1]

Best Overall Response and Duration of Response by Central Review

The ORR was 64.1% in the encorafenib + binimetinib arm, and 40.8% in the vemurafenib alone arm.[1,7]

- In the 7-year post-hoc analysis, the median duration of response with encorafenib + binimetinib was 18.6 months (95% CI: 12.7 to 27.6)[1,7]

Response Type	encorafenib + binimetinib (n=192)	vemurafenib (n=191)
Best overall response, n (%)[a, b]		
CR	29 (15.1)	16 (8.4)
PR	94 (49.0)	62 (32.5)
SD	44 (22.9)	71 (37.2)
Non-CR/Non-PD	10 (5.2)	6 (3.1)
PD	2 (1.0)	14 (7.3)
Unknown	12 (6.3)	22 (11.5)
Not assessed	1 (0.5)	0
Overall response rate, % (95% CI)[c]	**64.1 (56.8 to 70.8)**	**40.8 (33.8 to 48.2)**
Disease control rate, % (95% CI)[c]	**92.2 (87.4 to 95.6)**	**81.2 (74.9 to 86.4)**
Duration of response,[d] months, median (95% CI)[e]	**18.6 (12.7 to 27.6)**	**12.3 (6.9 to 14.5)**

Best Overall Response and Duration of Response by Central Review

Table adapted from Supplement to Schadendorf D, et al 2024[7]

[a]Best overall response is based on central reviewer's assessment using RECIST 1.1.[7]

[b]CR and PR are confirmed by repeat assessments performed not less than 4 weeks after the criteria for response is first met.[7]

[c]The 95% CI for the frequency distribution of each variable was computed using the Clopper-Pearson's method.[7]

[d]Responders are defined as patients achieving at least one confirmed CR or PR.[7]

[e]Percentiles with 95% CIs were calculated from PROC LIFETEST output using the Brookmeyer and Crowley method.[7]

What were the safety findings in the updated analysis?

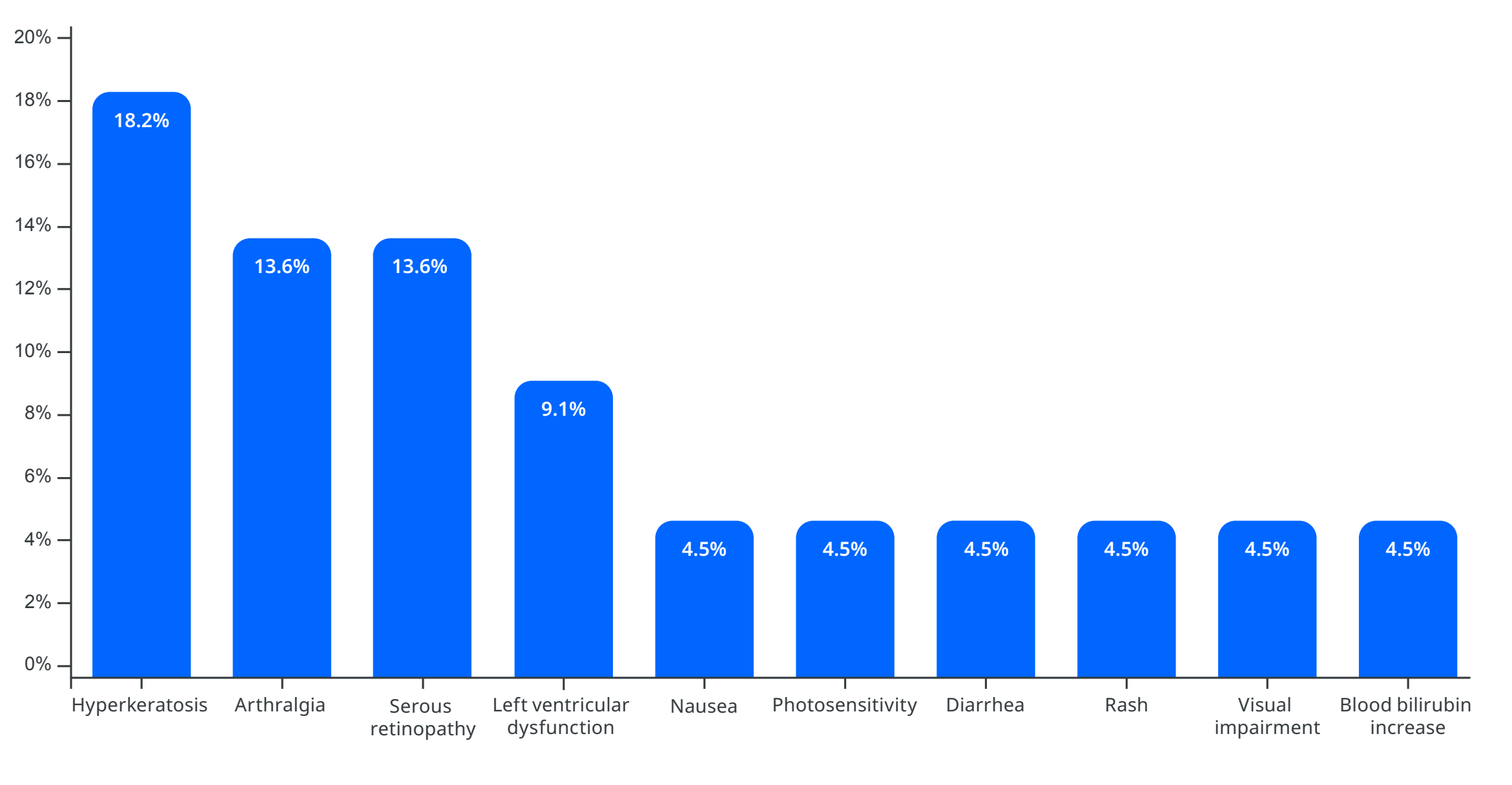
Safety results were consistent with the known safety and tolerability profile of encorafenib + binimetinib[1]

1 year

Most treatment-related AESIs occurred within the first year of treatment with encorafenib + binimetinib[1]

Treatment-related AESIs with incidence occurring after 7 years included arthralgia (4.5%), left ventricular dysfunction (4.5%) and rash (4.5%)[1]

Treatment-related AESIs with prevalence occurring after 7 years included:[1]



Response Type	encorafenib + binimetinib (n=192)		vemurafenib (n=191)	
Category	**All Grades**	**Grade 3/4**	**All Grades**	**Grade 3/4**
All deaths[a]	**139 (72.4)**		**145 (78.0)**	
On-treatment deaths[b]	26 (13.5)		20 (10.8)	
AEs	**189 (98.4)**	**135 (70.3)**	**186 (100)**	**122 (65.6)**
Suspected to be drug related	173 (90.1)	78 (40.6)	182 (97.8)	86 (46.2)
Serious AEs	**84 (43.8)**	**75 (39.1)**	**78 (41.9)**	**66 (35.5)**
Suspected to be drug related	24 (12.5)	17 (8.9)	26 (14.0)	22 (11.8)
AEs leading to discontinuation	**38 (19.8)**	**29 (15.1)**	**33 (17.7)**	**20 (10.8)**
Suspected to be drug related	21 (10.9)	13 (6.8)	26 (14.0)	14 (7.5)
AEs requiring dose interruption and/or adjustment	**109 (56.8)**	**75 (39.1)**	**116 (62.4)**	**74 (39.8)**
Suspected to be drug related	90 (46.9)	56 (29.2)	106 (57.0)	59 (31.7)
AEs requiring additional therapy[c]	**171 (89.1)**	**92 (47.9)**	**173 (93.0)**	**96 (51.6)**
Suspected to be drug related	123 (64.1)	32 (16.7)	162 (87.1)	57 (30.6)

Overall Summary of Deaths and Adverse Events in the Safety Population

Table adapted from Schadendorf D, et al 2024[1]

[a]All deaths, regardless of cause, including those occurring >30 days after the end of treatment.[1]

[b]Deaths occurring >30 days after the end of treatment are not included.[1]

[c]Additional therapy includes all non-drug therapy and concomitant medications.[1]

What were the key findings of the 7-year analysis of the COLUMBUS study?

Results support the long-term efficacy and known safety of encorafenib + binimetinib in patients with *BRAF* V600E/K-mutant unresectable or metastatic melanoma.[1]

In the 7-year post-hoc analysis:[1]
- – 27.4% of patients treated with encorafenib + binimetinib and 18.2% of patients treated with vemurafenib were alive
- – 21.2% of patients treated with encorafenib + binimetinib and 6.4% of patients treated with vemurafenib remained progression-free

Long-term safety results were consistent with the known tolerability profile of encorafenib plus binimetinib, and no new safety signals were observed.[1]

To find out more about the COLUMBUS 7-Year Update please see the full manuscript

By clicking the link above, you will be directed to a third party website. Links to other websites are provided as a convenience to the viewer. Pfizer accepts no responsibility for content of sites that are not owned and operated by Pfizer.

Abbreviations:

AE = adverse event; AESI = adverse event of special interest; AJCC = American Joint Committee on Cancer; BICR = blinded independent central review; BID = twice daily; CI = confidence interval; CR = complete response; DCR = disease control rate; DOR = duration of response; ECOG PS = Eastern Cooperative Oncology Group Performance Status; HR = hazard ratio; ORR = objective response rate; OS = overall survival; PD = progressive disease; PFS = progression-free survival; PK = pharmacokinetics; PR = partial response; QD = once daily; QoL = quality of life; RECIST = Response Evaluation Criteria in Solid Tumors; SD = stable disease; TTR = time to response.

References:
1. Schadendorf D, et al. *Eur J Cancer*. 2024;204:114073; 2. Dummer R, et al. *Lancet Oncol.* 2018;19(5):603-615; 3. Ascierto PA et al. *J Clin Oncol.* 2023;41(29):4621-4631; 4. Braftovi® (encorafenib) Prescribing Information. New York, NY: Pfizer Inc.; 2023; 5. Schadendorf D, et al. *Lancet.* 2018;392(10151):971-984; 6. Michielin O, et al. *Ann Oncol.* 2019;30(12):1884-1901; 7. Supplement to Schadendorf D, et al. *Eur J Cancer.* 2024;204:114073.