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5-year update on COLUMBUS: A randomized phase III trial of encorafenib (enco) + binimetinib (bini) versus enco or vemurafenib (vem) in patients (pts) with BRAF V600-mutant melanoma

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Background

Combined BRAF/MEK inhibitor therapy has demonstrated benefits on progression-free survival (PFS) and overall survival (OS) and is standard of care for the treatment (tx) of advanced *BRAF* V600-mutant (*BRAF*^{V600}) melanoma. Here we report additional data from the 5-year update of the ongoing COLUMBUS trial.

Methods

In COLUMBUS Part 1, 577 pts with advanced/metastatic *BRAF*^{V600} melanoma, untreated or progressed after first-line immunotherapy, were randomized 1:1:1 to enco 450 mg once daily + bini 45 mg twice daily, enco 300 mg once daily, or vem 960 mg twice daily. An updated analysis was conducted after 65 months' minimum follow-up. Data are as is.

Results

In the enco + bini arm, the 5-year OS rate (95% CI) in all pts (n=192), those with lactate dehydrogenase (LDH) ≤ upper limit of normal (ULN) at baseline (n=137), and low tumor burden (n=88) was 35% (28–42), 45% (36–53), and 48% (37–58), respectively (data cut-off: Sep 15, 2020). Other efficacy results are shown in the table. Safety results were consistent with the known tolerability profile of enco + bini. Adverse events (AEs) occurring in ≥ 20% of enco + bini pts were nausea, diarrhea, vomiting, arthralgia, fatigue, increased blood creatinine phosphokinase (CPK), headaches, constipation, asthenia, and pyrexia. Grade 3/4 AEs occurring in ≥ 2.5% of pts in the enco + bini were hypertension, pyrexia, abdominal pain, diarrhea, and vomiting. Grade 3/4 abnormal laboratory values occurring in ≥ 2.5% pts in the enco + bini arm were increased gamma-glutamyl transferase, increased blood CPK, anemia, increased alanine transaminase, and hyperglycemia. 12%–14% of pts in each arm discontinued tx due to AEs. The most common anti-cancer tx after enco + bini were checkpoint inhibitors. Additional analyses will be presented.Table: 1041MO

	Enco + bini (n=192)	Enco (n=194)	Vem (n=191)
5-year PFS rate*	23 (16–30)	19 (13–27)	10 (5–18)
5-year OS rate* LDH ≤ ULN n LDH > ULN	35 (28–42) 45 (36–53) 137	35 (28–42) 42 (33–50) 147	21 (16–28) 28 (21–36) 139
n Low tumor burden n	9 (3–18) 55 48 (37–58) 88	14 (6–26) 47 50 (39–60) 94	4 (1–12) 52 38 (28–49) 84
Objective response rate*	64 (57–71)	52 (44–59)	41 (34–48)
Disease control rate*	92 (87–96)	84 (78–89)	81 (75–86)
Complete response†	27 (14)	15 (8)	16 (8)
Partial response†	96 (50)	85 (44)	62 (32)
Stable disease† (includes non-complete response or non-progressive disease)	54 (28)	63 (32)	77 (40)
Progressive disease† (includes best response of unknown or no assessment)	15 (8)	31 (16)	36 (19)

*% (95% CI) †n (%)

% (95% CI) †††† (%)

Conclusions

Updated results with enco + bini indicate continued long-term benefit in pts with advanced/metastatic *BRAF*^{V600} melanoma.

Clinical trial identification

NCT01909453; release date: July 26, 2013.

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Pfizer.

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