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STARBOARD phase 3: A randomized, double-blind study of first-line (1L) encorafenib (enco), binimetinib (bini), and pembrolizumab (pembro) vs placebo (pbo) and pembro for unresectable locally advanced or metastatic BRAF V600-mutant melanoma

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Background

About half of patients (pts) with metastatic melanoma have *BRAF* V600 mutations. For these pts, the current standard of care is immune checkpoint inhibitors (ICI; eg pembro [anti-PD-1]) or other immunotherapy combinations and often does not include BRAF/MEK inhibitors (BRAF/MEKi). In the safety lead-in portion of STARBOARD, the combination of enco (BRAFi), bini (MEKi), and pembro was generally tolerable with a favorable response rate. Here, from STARBOARD phase 3, is the final analysis of ORR and PFS by blinded independent central review (BICR), OS and safety.

Methods

Eligible pts had histologically confirmed metastatic or unresectable cutaneous melanoma with *BRAF* V600E/K mutation, measurable disease (RECIST 1.1), ECOG PS 0-1, and had not received 1L systemic therapy. Pts were randomized 1:1 to receive enco, bini, and pembro (triplet) or pbo and pembro (control) and were stratified by prior adjuvant therapy and stage of disease. The primary endpoint (EP) was ORR by BICR. PFS by BICR was a key secondary EP; other secondary EPs included OS and safety.

Results

In 220 pts (cutoff: Jan 12, 2026), baseline characteristics were similar across arms. Both primary and key secondary EPs were met (Table); confirmed ORR was 70.0% (triplet) vs 32.7% (control); median PFS was 33.0 vs 3.4 mo, respectively, and risk of disease progression or death was reduced by 67% for triplet vs control. OS was immature but showed a positive trend favoring triplet vs control. No new safety signals and no grade 5 treatment-related TEAEs were observed. Grade 3/4 TEAEs were reported in 70% (triplet) vs 39% (control) of pts.Table: 20710

	Triplet n=110	Control n=110
Confirmed ORR ^a (95% CI), %	70.0 (60.9, 77.8)	32.7 (24.7, 41.9)
Odds ratio (90% CI)	4.90 (2.87, 8.13) <i>P</i> -value ^b <0.0001	
Median PFS ^a (95% CI), mo	33.0 (20.0, NE)	3.4 (2.2, 8.3)
Hazard ratio (90% CI)	0.33 (0.24, 0.46) <i>P</i> -value ^b <0.0001	
Estimated 12-mo PFS (95% CI), %	71 (60, 79)	34 (25, 44)

	Triplet n=110	Control n=110
Estimated 24-mo PFS (95% CI), %	55 (44, 65)	26 (18, 35)
Median OS (95% CI), mo	NE (NE, NE)	NE (31.8, NE)
Hazard ratio (90% CI)	0.71 (0.48, 1.05)	
Estimated 12-mo OS (95% CI), %	90 (82, 94)	79 (70, 86)
Estimated 24-mo OS (95% CI), %	77 (67, 84)	64 (54, 73)
Median duration of treatment (range), wk 69 (<1, 170)		30 (3, 185)

^aBy BICR. ^bOne-sided. NE, not estimable.

Conclusions

STARBOARD demonstrated meaningful, statistically significant clinical benefit with enco, bini, and pembro vs pbo + pembro; safety was consistent with known profiles of regimen components.

Clinical trial identification

NCT04657991.

Editorial acknowledgement

Medical writing support was provided Eleanor Porteous, MSc, of Nucleus Global, an Inizio Company, and was funded by Pfizer.

Legal entity responsible for the study

This study was sponsored by Pfizer in collaboration with Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, USA.

Funding

This study was sponsored by Pfizer in collaboration with Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, USA.

Disclosure

D. Schadendorf: Financial Interests, Personal, Invited Speaker: BMS, MSD, Merck Serono, Regeneron, Pierre Fabre; Financial Interests, Personal, Advisory Board: BMS, Novartis, MSD, Immunocore, Pierre Fabre, Regeneron, Philogen, BioAlta, Daiichi Sankyo, BioNTech, Immatics, Formycon, Replimune, Sun Pharma, Skyline Dx, IOVance, Ipsen, IOBioTech, Boehringer Ingelheim, Imcheck, Moderna, EeBeTe, Incyte; Financial Interests, Institutional, Coordinating PI: BMS, MSD, Pierre Fabre, Immatics; Financial Interests, Institutional, Research Grant: BMS, MSD; Financial Interests, Personal, Steering Committee Member: MSD; Financial Interests, Institutional, Local PI: Philogen, Immunocore, Regeneron, Biontech Rna Pharmaceuticals GMBH, Replimune, IO Biotech; Non-Financial Interests, Member of Board of Directors: EORTC-MG; Non-Financial Interests, Leadership Role, Founding member and SC chair: European Melanoma Registry (EuMelaReg). R. Dummer: Financial Interests, Personal, Other, Consulting and/or advisory role: Novartis, Merck Sharp & Dohme (MSD), Bristol Myers Squibb (BMS), Roche, Amgen, Takeda, Pierre Fabre, Sun Pharma, Sanofi, Catalym, Second Genome, Regeneron, MaviVAX SA, T3 Pharma, Pfizer, Simcere, Iovance Biotherapeutics; Financial Interests, Personal, Other, medical advisor: Oncobit; Financial Interests, Personal, Other, Participation on Derma2go: Derma2go. R.J. Sullivan: Financial Interests, Personal, Advisory Board, Advisory board/consultancy: MSD; Financial Interests, Personal, Other, Consultant: Marengo; Financial Interests, Personal, Advisory Board, Consultancy/SAB: Novartis; Financial Interests, Personal, Other, Consultancy: Pfizer, Replimune; Financial Interests, Personal, Advisory Board: PharmaMar; Financial Interests, Personal, Royalties: Up-to-Date; Financial Interests, Institutional, Coordinating PI, Phase 1 trial PI: Marengo; Financial Interests, Institutional, Local PI: Novartis, Synthekine, Immunocore, Springworks, Biontech Rna Pharmaceuticals GMBH; Financial Interests, Institutional, Coordinating PI: Mural, Moderna, Georgiamune, Erasca; Financial Interests, Institutional, Steering Committee Member: Merck. C. Robert: Financial Interests, Personal, Advisory Board, Consultancy fees: BMS, Roche, Pierre Fabre, MSD, Pfizer, Sun Pharma, Merck, Regeneron, Maat Pharma, Iovance Biotherapeutics, Moderna Therapeutics, Immunitas Therapeutics; Financial Interests, Personal, Invited Speaker: Pierre Fabre, BMS, MSD; Financial Interests, Personal, Other, Steering Committee: Regeneron, Pfizer, IO Biotech. A. Ribas: Financial Interests, Personal, Advisory Board, Honoraria for consulting: Amgen, Merck; Financial Interests, Personal, Advisory Board, Member of the Scientific Advisory Board: Arcus, Compugen, Dispatcgh, Lutris, Lyell, Synthekine, Tango; Financial Interests, Personal, Member of Board of Directors, Member of the Board of Directors: Arcus, Lutris; Financial Interests, Personal, Advisory Board: Arsenal Bio; Non-Financial Interests, Advisory Role, Member of the scientific advisory board: Highlight, Immunesensor, Inspirna, Pluto. P.A. Ascierto: Financial Interests, Personal, Other, Consultant and Advisory Role: BMS, Roche Genentech, Novartis, Merck Serono, Sun Pharma, Immunocore, Boehringer Ingelheim, Regeneron; Financial Interests, Personal, Other, Consultant, Advisory Role and Travel support: MSD, Pierre Fabre; Financial Interests, Personal, Other, Consultant and Advisory Role.Travel support: Pfizer/Array; Financial Interests, Personal, Other, Consultant Role: Italfarmaco; Financial Interests, Personal, Other, Consultant Role: Pfizer, Nouscom; Financial Interests, Personal, Other, Consultant role: Medicenna; Financial Interests, Personal, Other, Consultant role and travel support: Bio-AI Health; Financial Interests,

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