**Background**

In the dabrafenib + trametinib arm, 3- and 4-year RFS rates were 59% and 54%, respectively. In the dabrafenib + trametinib arm, 3- and 4-year DMFS rates were 71% and 61%, respectively.

*A* rate of tumor relapse was 15% absolute increase in the proportion of patients who will remain disease-free long term.

*An* interim analysis of overall survival showed a clinically meaningful improvement with dabrafenib + trametinib vs placebo (HR, 0.57 [95% CI, 0.40-0.76]).

The safety profile of the combination was consistent with that observed in patients with metastatic melanoma.

Based on those findings, dabrafenib + trametinib has been approved by multiple regulatory agencies globally, including the US Food and Drug Administration and European Commission, for the treatment of patients with the new primary melanoma.

**Methods**

**COMBI-AD** was a randomized, phase 3 study of dabrafenib + trametinib in patients with completely resected stage IIIB IV and IIIC melanoma (Figure 1).

**Data Set**

- Analyses were based on the data cutoff date for an updated analysis of the COMBI-AD study (April 30, 2016).
- Median follow-up was 40 months for 875 enrolled patients (dabrafenib + trametinib, n = 438; placebo, n = 437).

**Results**

- The median age of patients in COMBI-AD was 51 years. Kaplan-Meier analysis of RFS benefit favored dabrafenib + trametinib vs placebo regardless of age (Figure 2). Age > 51 years: Median RFS was not reached in the dabrafenib + trametinib arm vs 211 months in the placebo arm (HR, 0.51 [95% CI, 0.34-0.75]). Age ≤ 51 years: Median RFS was not reached in the dabrafenib + trametinib arm vs 15.8 months in the placebo arm (HR, 0.49 [95% CI, 0.38-0.64]).

- RFS benefit consistently favored dabrafenib + trametinib vs placebo across all 7 stages classified per AJCC 7th edition criteria (Figure 4).
- T1: Median RFS was not reached in the dabrafenib + trametinib arm vs 211 months in the placebo arm (HR, 0.42 [95% CI, 0.25-0.70]).
- T2: Median RFS was not reached in the dabrafenib + trametinib arm vs 221 months in the placebo arm (HR, 0.51 [95% CI, 0.34-0.76]).
- T3: Median RFS was 44.5 months in the dabrafenib + trametinib arm vs 9.6 months in the placebo arm (HR, 0.35 [95% CI, 0.19-0.67]).
- T4: Median RFS was 40.9 months in the dabrafenib + trametinib arm vs 8.6 months in the placebo arm (HR, 0.42 [95% CI, 0.29-0.65]).

**Conclusions**

- RFS benefit favored dabrafenib + trametinib in patients with completely resected stage IIIA BRAF V600E/K–mutant melanoma vs placebo regardless of the following baseline factors, confirming previous findings:
  - Sex
  - T stage
  - Histological subtype

- This updated analysis supports the use of dabrafenib + trametinib in a broad range of clinical and pathological contexts of patients at treatment indication.

**References**

7. Durmuz R et al. ESMO 2016 (poster 5625).

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**Figure 2**: Investigator-Assessed Kaplan-Meier RFS Curves by Age

**Figure 3**: Investigator-Assessed Kaplan-Meier RFS Curves by Sex

**Figure 4**: Investigator-Assessed Kaplan-Meier RFS Curves by Histological Subtype (superficial spreading, nodular, other)

**Figure 5**: Investigator-Assessed Kaplan-Meier RFS Curves by Stage

**Figure 6**: Investigator-Assessed Kaplan-Meier RFS Curves by Status of In-Transit Metastases

**Figure 7**: Investigator-Assessed Kaplan-Meier RFS Curves by New Primary Melanoma