cancers

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*Article*

# *TERT* Promoter Mutation as an Independent Prognostic Marker for Poor Prognosis MAPK Inhibitors-Treated Melanoma

**Pauline Blateau, Etienne Coyaud, Estelle Laurent, Benoit Béganton, Vincent Ducros, Géraldine Chauchard, Julie A. Vendrell and Jérôme Solassol**

## Supplementary Materials

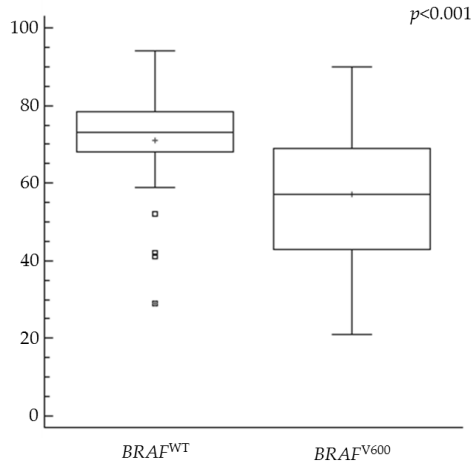


**Figure S1.** Age repartition in *BRAF*$^{V600}$ and *BRAF*$^{WT}$ samples.

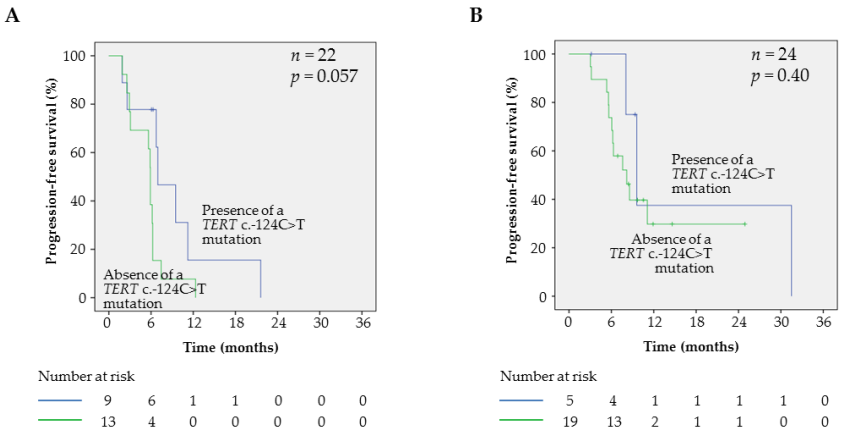


**Figure S2.** Effect of *TERT* c.-124C>T promoter mutation on clinical outcome of *BRAF*$^{V600}$ patients with elevated or normal LDH level. (**A**) Kaplan-Meier analysis of PFS in patients with elevated LDH level in function of the *TERT* c.-124C>T promoter mutation status. (**B**) Kaplan-Meier analysis of PFS in patients with normal LDH level in function of the *TERT* c.-124C>T promoter mutation status.

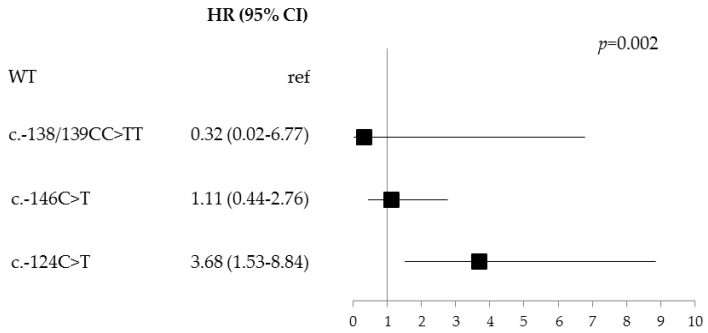


**Figure S3.** Univariate analysis of *TERT* promoter mutations with regard to OS in *BRAF*$^{V600}$ samples**.** Forest plot showing the hazard ratio for PFS associated to *TERT* promoter mutational status. *TERT* wild type (WT) samples were taken as reference (ref).

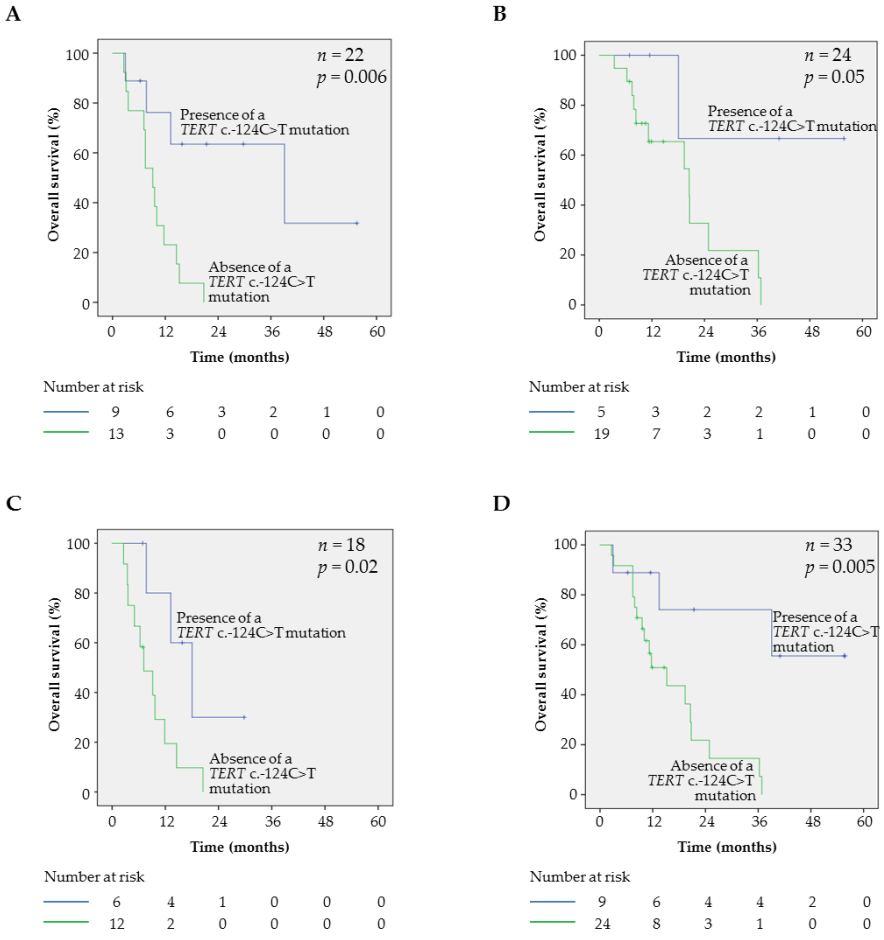


**Figure S4.** Effect of *TERT* c.-124C>T mutation on OS of *BRAF*$^{V600}$ patients depending on LDH level and brain metastasis presence. (**A**) Kaplan-Meier analysis of OS in patients with elevated LDH level in function of the *TERT* c.-124C>T promoter mutation status. (**B**) Kaplan-Meier analysis of OS in patients with normal LDH level in function of the *TERT* c.-124C>T promoter mutation status. (**C**) Kaplan-Meier analysis of OS in patients with brain metastasis in function of the *TERT* c.-124C>T promoter mutation status. (**D**) Kaplan-Meier analysis of OS in patients without brain metastasis in function of the *TERT* c.-124C>T promoter mutation status.

**Table S1.** Cohort clinicopathological features.

| Clinicopathological features | | *n* (%) |
|---|---|---|
| Age | <60 | 32 (36.0) |
| | >60 | 57 (64.0) |
| Sex | Male | 50 (56.2) |
| | Female | 39 (43.8) |
| Histological type | NM | 18 (22.8) |
| | SSM | 39 (49.4) |
| | MUP | 12 (15.2) |
| | Unclassified | 3 (3.8) |
| | ALM | 7 (8.9) |
| | Missing data | 10 |
| Primary tumor site | Head/neck | 18 (20.7) |
| | Upper limbs | 6 (6.9) |
| | Trunk | 27 (31.0) |
| | Lower limbs | 17 (19.6) |
| | MUP | 12 (13.8) |
| | Acral | 7 (8.0) |
| | Missing data | 2 |
| Breslow thickness* | <1 mm | 5 (7.2) |
| | 1–1.99 mm | 15 (21.7) |
| | 2–3.99 mm | 17 (24.6) |
| | ≥4 mm | 32 (46.4) |
| | Missing data | 8 |
| Clark level* | II | 2 (3.0) |
| | III | 12 (18.2) |
| | IV | 41 (62.1) |
| | V | 11 (16.7) |
| | Missing data | 11 |
| AJCC | I | 10 (11.9) |
| | II | 33 (39.3) |
| | III | 19 (22.6) |
| | IV | 22 (26.2) |
| | Missing data | 5 |

**Table S2.** Clinical prognostic factors and targeted therapy modalities in *BRAF*$^{V600}$ samples.

| **Clinical Prognostic Factors** | ***BRAF*$^{V600}$** | **(*n* = 53) (%)** |
|---|---|---|
| AJCC stage at the initiation of MAPK inhibitor | III | 6 (11.3) |
| | IV | 47 (88.7) |
| Number of metastasis | 0 | 8 (15.1) |
| | 1 | 2 (3.8) |
| | 2 | 2 (3.8) |
| | 3 | 6 (11.3) |
| | 4 | 2 (3.8) |
| | ≥5 | 33 (62.3) |
| Brain metastasis | Absence | 35 (66.0) |
| | Presence | 18 (34.0) |
| LDH | Normal | 25 (52.1) |
| | Elevated | 23 (47.9) |
| Targeted therapy modalities | | |
| BRAFi monotherapy | Vemurafenib | 4 (7.7) |
| | Dabrafenib | 2 (3.8) |
| BRAFi and MEKi bitherapy | Vemurafenib–Cobimetinib | 4 (7.7) |
| | Dabrafenib–Trametinib | 42 (80.8) |

AJCC: American Joint Committee on Cancer, MAPK: Mitogen-Activated Protein Kinases.

**Table S3.** Samples characteristics.

| Tumoral Status | *n* (%) | Median Tumor Content (Min-Max) | Samples Obtained Pre-treatment *n* (%) |
|---|---|---|---|
| All | 89 (100) | 80% (30–100) | 84 (94.4) |
| Primary tumor | 36 (40.4) | 75% (30–90) | 36 (100.0) |
| Metastasis | 53 (59.6) | 80% (30–100) | 48 (90.6) |

**Table S4.** NGS panel.

| Gene | Exons | Reference Transcripts |
|---|---|---|
| *AKT1* | 3 | (NM_001014431) |
| *ALK* | 20, 21, 22, 23, 24, 25 | (NM_004304) |
| *BRAF* | 11, 15 | (NM_004333) |
| *CDKN2A* | 1, 2, 3 | (NM_000077) |
| *CTNNB1* | 3 | (NM_001904) |
| *DDR2* | 17 | (NM_006182) |
| *EGFR* | 18, 19, 20, 21 | (NM_005228) |
| *ERBB2* | 20 | (NM_004448) |
| *ERBB4* | 10, 12 | (NM_005235) |
| *FGFR1* | 12, 14 | (NM_023110) |
| *FGFR2* | 7, 12, 14 | (NM_000141) |
| *FGFR3* | 7, 9, 14 | (NM_000142) |
| *GNA11* | 4, 5 | (NM_002067) |
| *GNAQ* | 5 | (NM_002072) |
| *GNAS* | 8, 9 | (NM_000516) |
| *H3F3A* | 2 | (NM_002107) |
| *H3F3B* | 2 | (NM_005324) |
| *HIST1H3B* | 1 | (NM_003537) |
| *HRAS* | 2, 3, 4 | (NM_005343) |
| *IDH1* | 4 | (NM_005896) |
| *IDH2* | 4 | (NM_002168) |
| *JAK2* | 12, 13, 14 | (NM_004972) |
| *KIT* | 8, 9, 11, 13, 17, 18 | (NM_000222) |
| *KRAS* | 2, 3, 4 | (NM_033360) |
| *MAP2K1* | 2 | (NM_002755) |
| *MET* | 2, 14, 15, 16, 17, 18, 19, 20 | (NM_001127500) |
| *NRAS* | 2, 3, 4 | (NM_002524) |
| *PDGFRA* | 12, 14, 18 | (NM_006206) |
| *PIK3CA* | 10, 21 | (NM_006218) |
| *POLE* | 9, 10, 11, 12, 13, 14 | (NM_006231) |
| *PTEN* | 1, 2, 3, 4, 5, 6, 7, 8, 9 | (NM_000314) |
| *RAC1* | 2 | (NM_018890) |
| *SMAD4* | 2, 3, 9, 10, 11, 12 | (NM_005359) |
| *STK11* | 1, 2, 3, 4, 5, 6, 7, 8, 9 | (NM_000455) |
| *TERT* | Promoter | – |