Oncogenic *BRAF* mutation in cutaneous melanoma in Argentina

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Background

BRAF is a critical protein in the mitogen-activated protein kinase (MAPK) pathway, and is mutated in approximately 50% of melanoma patients[1]. A single substitution (V600E) account for 80% of BRAF mutations[2-3]. Trunck location, age at diagnosis of primary tumor ≤ 50 years and the absence of chronic sun damage predict relationship between primary melanoma and Braf mutation.[6,7]

Objective

The aim of this study was to assess the frequency of oncogenic *BRAF* mutations in cutaneous melanoma and to correlate *BRAF* status with clinic-pathological features in Argentinian melanoma patients.

Patients and Methods: Tumor tissue from 92 consecutive patients with primary/metastatic cutaneous melanoma, from 12/2011 to 3/2013 was analyzed in 2 referral centers using real time polymerase chain reaction (RT-PCR) assays for *BRAF* mutation (cobas® 4800 System, v2.0)[4] .
Clinical (age, gender, ethnics, primary tumor location) and pathological (Breslow, ulceration, histo-pathological subtype, mitotic rate, AJCC stage) features were correlated with BRAF mutational status

Inclusion criteria: > 18 yrs, histology confirmed cutaneous melanoma (any TNM stage), available tissue for mutational analysis (primary, lymph node or metastasis).

Exclusion criteria: Uveal, mucosal or acral melanoma.

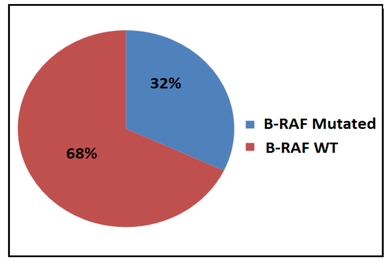
Results

Patient/Tumor Characteristics	N= 92 (%)
Age at diagnosis. Median (range)	58 (17-96) < 35: 17 (18%) 36-50: 20 (31%) 51-70: 34 (36%) >71: 26 (28%)
Sex	47 *Males* (51%)
Gender	92 *caucasian* (100%)
Primary tumor location	35 *Trunk/Back* (38%) 31 *Extremities* (33%) 14 *Other* (15%) 10 *Head and Neck* (10%) 2 *Unknown* (2%)
Breslow (mm)	≤ 1: 23 (25%) 1,01 a 2: 18 (19%) 2,01 a 3: 10 (10%) 3,01 a 4: 7 (7%) ≥4,01: 15 (16%) Unknown: 19 (20%)

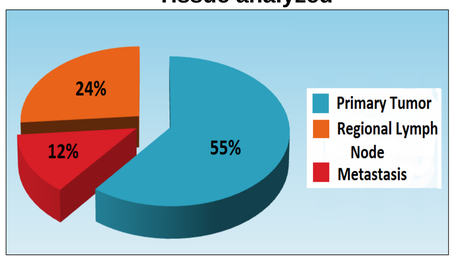
Patient/Tumor Characteristics	N= 92 (%)
Mitotic Index (per mm²)	*≤ 1mm²*: 31 (33%) *≥ 1 mm²*: 32 (34%) *Unknown*: 29 (31%)
Ulceration	*Yes*: 18 (19%) *No*: 45 (48%) *Unknown*: 29 (31%)
Vascular Invasion	*Yes*: 19 (20%) *No*: 36 (39%) *Unknown*: 37 (40%)
Spontaneus regression	*Yes*: 3 (3%) *No*: 56 (60%) *Unknown*: 33 (35%)
Stage	*Localized*: 52 (56%) *Locally advanced*: 20 (22%) *Metastasic* : 20(22%)

Comparison of 92 patients with BRAF WT (32%) and BRAF mut (68%) found a statistically significant association with **age at diagnosis** (p = .001; Student's Test) and **ulceration** (p = .005; Mann-Withney's Test) only.

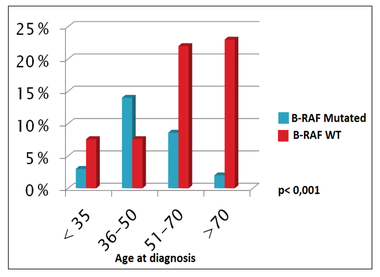
Mutation results



Tissue analyzed



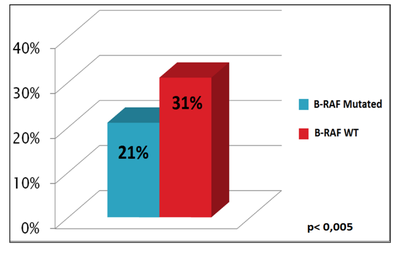
Age at diagnosis



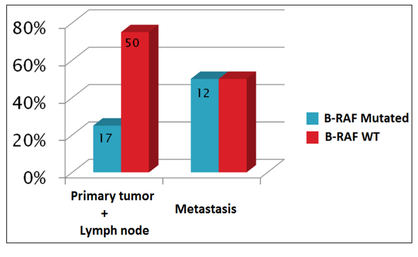
Median age at diagnosis (range)

Mutated	Wild Type
51 years (23-85)	**62 years** (17-96)

Ulceration



Mutation status according to tissue analysed



Conclusions

This is the first report of BRAF mutation status using RT-PCR COBAS in Argentina. The frequency of BRAF mutation is lower than that reported in medical literature, and only the presence of ulceration and age at diagnosis were significantly different in *BRAF*-mutant and *BRAF* wild-type patients. Future studies with more number of patients will clarify our observation.

References

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