The Prognostic Value of *BRAF* Gene Mutation in Melanoma and colorectal Cancer: A Systematic Review and Meta-analysis

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BRAF mutations and MAPK pathway

- 7% of Cancers
- 60% of Melanoma

Chin L. Nat Rev Cancer. 2003 Aug;3(8):559-70

Schubbert S. Nat Rev Cancer. 2007 Apr;7(4):295-308
## BRAF mutation in different cancers

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Melanoma</td>
<td>50-60%</td>
</tr>
<tr>
<td>Papillary thyroid carcinoma</td>
<td>40%</td>
</tr>
<tr>
<td>Ovarian Cancer</td>
<td>15-30%</td>
</tr>
<tr>
<td>Colangiocarcinoma</td>
<td>20%</td>
</tr>
<tr>
<td>Colorectal Cancer</td>
<td>15-20%</td>
</tr>
<tr>
<td>NSCLC</td>
<td>3%</td>
</tr>
</tbody>
</table>

Targeting *BRAF-V600E* for melanoma treatment and its complications

**BRAF** mutation & patient survival

The correlation between *BRAF-V600E* mutation and cancer patient survival is still a matter of controversy in different reports.

- Reports with **negative** effect
- Reports with **no difference**
- And even reports for **protective effect** on patient survival
What we did?

• We searched MEDLINE and EMBASE using the terms “BRAF”, “BRAF mutation”, “BRAF V600E”, “cancer”, “patient survival”, “colorectal cancer”, “melanoma”, and “papillary thyroid carcinoma” in different combinations from June 2002 to December 2011.

• 120 relevant full text studies were categorized based on study design and cancer type.
Study Selection Process

Records identified based on first data base search, n=565

Excluded based on title and abstract, n=445

Full-text reviewd, n=120

Excluded studies based on full-text review
- Review, n=16
- Letters or comments, n=2
- Case series, n=1
- Studies on cell line and animal studies, n=10
- Studies with no data on BRAF survival, n=39
- Studies with non-extractable data about BRAF survival, n=15
- Studies from same center, n=4

Studies included after reference check and final search, n=7

Studies on papillary thyroid carcinoma, n=10
Total number of studies in final meta-analysis
- Colorectal cancer, n=26
- Melanoma, n=4
Studies included in final Meta-Analysis

- Colorectal Cancer: 26 studies
- Melanoma: 10 studies
- Papillary Thyroid Carcinoma: 4 studies
Colorectal Cancer Patient Survival

Heterogeneity was significant \((P < 0.0001)\)

\(I^2\) estimate of variation between analyzed studies was 74.3\%.
Colorectal Cancer Patient Survival

26 studies (11,773 patients) HR 2.24 (1.82-2.83, 95% CI)
Heterogeneity was not significant ($P = 0.467$)
$I^2$ estimate of variation between analyzed studies was 0.0%.
Melanoma Patient Survival

4 studies (674 patients) HR of 1.70 (1.37-2.12, 95% CI)
## Papillary Thyroid Carcinoma

<table>
<thead>
<tr>
<th>Study</th>
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<tbody>
<tr>
<td><strong>Overall</strong></td>
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<tr>
<td></td>
</tr>
<tr>
<td>Abubaker J [26]</td>
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<tr>
<td>Costa AM [27]</td>
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<td>Elisei R [20]</td>
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<td>Ito Y [25]</td>
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<td>Musholt TJ [18]</td>
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<td>Oler G [75]</td>
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<td>O’Neill CJ [24]</td>
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<td>Stanojevic B [10]</td>
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<td>Wang W [28]</td>
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<tr>
<td>Xing M [76]</td>
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### Notes:
- **BRAF** mutant
- **BRAF** WT
- DFS: Disease-free survival
- OR: Odds ratio
- *P*: Probability
- **SBiPTC**: Somatic BRAF mutation in papillary thyroid cancer
- **UiPTC**: Unique BRAF mutation in papillary thyroid cancer
Take home message

- *BRAF-V600E* mutation increases the risk of mortality in *Colorectal Cancer* patients for more than two-fold.
- This mutation also significantly increases the risk of mortality in *melanoma* patients (HR: 1.7).
- Data on *papillary thyroid carcinoma* are not conclusive enough and studies with larger sample size are required.
- There is *Hope* that with successful *BRAF* inhibition we could increase patient survival.
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- All my lab members

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