Development and validation of a combined hypoxia and immune prognostic classifier for head and neck cancer

Brooks, Jill; Antao Mobre De Menezes, Albert Rahul Eugene; Ibrahim, Maha; Archer, Lucinda; Lal, Neeraj; Bagnall, Chris; Zeidler, Sandra Ventorin von; Valentine, Helen; Spruce, Rachel; Batis, Nikolaos; Bryant, Jennifer; Hartley, Margaret; Kaul, Baksho; Ryan, Gordon; Bao, Riyue; Khattri, Arun; Lee, Steve; Ogbureke, Kalu U.E.; Middleton, Gary; Tennant, Daniel

DOI: 10.1158/1078-0432.CCR-18-3314

License:
None: All rights reserved

Document Version
Peer reviewed version

Citation for published version (Harvard):

Link to publication on Research at Birmingham portal

Publisher Rights Statement:

General rights
Unless a licence is specified above, all rights (including copyright and moral rights) in this document are retained by the authors and/or the copyright holders. The express permission of the copyright holder must be obtained for any use of this material other than for purposes permitted by law.

- Users may freely distribute the URL that is used to identify this publication.
- Users may download and/or print one copy of the publication from the University of Birmingham research portal for the purpose of private study or non-commercial research.
- Users may use extracts from the document in line with the concept of ‘fair dealing’ under the Copyright, Designs and Patents Act 1988 (?).
- Users may not further distribute the material nor use it for the purposes of commercial gain.

Where a licence is displayed above, please note the terms and conditions of the licence govern your use of this document.

When citing, please reference the published version.

Take down policy
While the University of Birmingham exercises care and attention in making items available there are rare occasions when an item has been uploaded in error or has been deemed to be commercially or otherwise sensitive.

If you believe that this is the case for this document, please contact UBIRA@lists.bham.ac.uk providing details and we will remove access to the work immediately and investigate.

Download date: 26. Apr. 2021
Figure 1

A

B

C

D

E

F

Figure 1

Overall survival

Time (months)

Non-adjusted=10.08 on 1 df, p=0.012
HPV-adjusted=15.08 on 2 df, p=0.0005

Non-adjusted=10.08 on 1 df, p=0.012
HPV-adjusted=15.08 on 2 df, p=0.0005

Non-adjusted=2.76 on 1 df, p=0.097
p16-adjusted=15.49 on 2 df, p=0.0003

Non-adjusted=10.08 on 1 df, p=0.012
HPV-adjusted=15.08 on 2 df, p=0.0005

Non-adjusted=10.08 on 1 df, p=0.012
HPV-adjusted=15.08 on 2 df, p=0.0005

Non-adjusted=10.08 on 1 df, p=0.012
HPV-adjusted=15.08 on 2 df, p=0.0005

Non-adjusted=10.08 on 1 df, p=0.012
HPV-adjusted=15.08 on 2 df, p=0.0005
Figure 2

Hypoxia markers

<table>
<thead>
<tr>
<th>Gene</th>
<th>CA9</th>
<th>FOSL1</th>
<th>HILPDA</th>
<th>MRGBP</th>
<th>SLC2A1</th>
<th>SLC16A1</th>
<th>VEGFA</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

T cell phenotypic and functional markers

<table>
<thead>
<tr>
<th>Gene</th>
<th>CD3E</th>
<th>CD4</th>
<th>TBX21</th>
<th>FOXP3</th>
<th>CD8B</th>
<th>PRF1</th>
<th>GZMB</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Myeloid lineage phenotypic and functional markers

<table>
<thead>
<tr>
<th>Gene</th>
<th>CD14</th>
<th>CD33</th>
<th>CD68</th>
<th>CD163</th>
<th>ORL1</th>
<th>ARG1</th>
<th>NOS2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Activating immune receptors

<table>
<thead>
<tr>
<th>Gene</th>
<th>CD27</th>
<th>CD40</th>
<th>CD80</th>
<th>ICOS</th>
<th>TNFRSF4</th>
<th>TNFRSF9</th>
<th>EGFR</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Inhibitory immune receptors/ligands

<table>
<thead>
<tr>
<th>Gene</th>
<th>CTLA4</th>
<th>HAVCR2</th>
<th>LAG3</th>
<th>PDCD1</th>
<th>CD274</th>
<th>ENTPD1</th>
<th>NTSE</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Immune modulators

<table>
<thead>
<tr>
<th>Gene</th>
<th>'IFNγ signature'</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

CXCL9 | CXCL10 | HLADRA | IDO1 | IFNG | STAT1 |

- hypoxia\text{low}immune\text{high}
- hypoxia\text{high}immune\text{low}
- mixed
Figure 3

A. TILs

B. CD3

C. PD-L1

D. LAG3

E. CA-IX

F. Overall survival

G. Overall survival

H. Overall survival

I. Overall survival

J. Overall survival
Figure 4

A

<table>
<thead>
<tr>
<th>Gene</th>
<th>TILs</th>
<th>CD3</th>
<th>LAG3</th>
<th>PD-L1 tumour</th>
<th>PD-L1 IC</th>
<th>CA-IX</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td></td>
<td>0.0055</td>
<td>0.002</td>
<td>0.0266</td>
<td>0.2336</td>
<td>0.7201</td>
<td>0.0012</td>
</tr>
<tr>
<td></td>
<td>0.1213</td>
<td>0.0014</td>
<td>0.1309</td>
<td>0.0085</td>
<td>0.0217</td>
<td>0.0364</td>
</tr>
</tbody>
</table>

B

- Immune desert
- Immune excluded
- Inflamed

p <0.0001
Figure 5

A

Hypoxia\textsubscript{high}/immune\textsubscript{low} CA-IX

PD-L1

B

Mixed CA-IX

PD-L1

C

Hypoxia\textsubscript{high}/immune\textsubscript{low} CA-IX

PD-L1

D

\begin{align*}
    r &= -0.5464 \\ p &= 0.0377 \\
    r &= -0.2393 \\ p &= 0.3982 \\
    r &= -0.4571 \\ p &= 0.0888
\end{align*}

E

\begin{align*}
    r &= 0.3464 \\ p &= 0.2061 \\
    r &= 0.7286 \\ p &= 0.0029 \\
    r &= 0.5 \\ p &= 0.0602
\end{align*}