DC vaccination concurrently reduces Tregs and enhances activated CTLs in tumor biopsies from immunoresponsive patients with advanced melanoma


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- 12 PD, 2 CR, 8 PR, 5 SD (according to irRC);
- OR 37.03%;
- Clinical Benefit: 55.5%.

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- 12 PD, 2 CR, 8 PR, 5 SD (according to irRC);
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All clinical responders were also immunological responders (positive DTH to KLH and autologous tumor lysate and/or positive ELISPOT).
Survival

Log rank = 7.26, P = 0.007

<table>
<thead>
<tr>
<th></th>
<th>Number of patients</th>
<th>Number of events (%)</th>
<th>Median survival (95% CI)</th>
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</thead>
<tbody>
<tr>
<td>DTH negative</td>
<td>8</td>
<td>7 (87.5)</td>
<td>4.8 (3.9–11.9)</td>
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<tr>
<td>DTH positive</td>
<td>19</td>
<td>12 (63.2)</td>
<td>22.9 (13.4–61.3)</td>
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</table>

Number of patients at risk

<table>
<thead>
<tr>
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<th>Months</th>
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<td>DTH Neg</td>
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</tr>
<tr>
<td></td>
<td>3</td>
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<tr>
<td>DTH Pos</td>
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<td>7</td>
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<td>5</td>
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</tbody>
</table>
.... why do immunoresponsive patients fail under DC vaccination??
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Answer 1

Vaccine-induced immunological pressure select for lower immunogenic tumor cells variants (defects in Ag processing/presentation).
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**Question**

Increased levels of FOXP3+ regulatory T cells have been observed in vaccine injection as well as in DTH sites after repeated administration of peptide or DC vaccines: is it true also for tumor sites?
Sixteen melanoma biopsies taken by 8 patients before and after at least 5 DC vaccine courses (all immunological responders)
Sixteen melanoma biopsies taken by 8 patients before and after at least 5 DC vaccine courses (all immunological responders)

*Immunohistochemistry for:*

- CD3
- CD8
- Granzyme B
- FOXP3
Digital camera acquisition

Computer-assisted counting

ImageJ
Image Processing and Analysis in Java

RSB
Research Services Branch
National Institute of Mental Health
National Institute of Neurological Disorders and Stroke
FOXP3+ TILs (nr/100 tumor cells)
p=0.031

Legend:
- GD
- BF
- MJL
- CK
- AL
- BI
- CE
- SL

Prevax vs. Postvax
<table>
<thead>
<tr>
<th>Protein</th>
<th>Prevax</th>
<th>Postvax</th>
<th>Postvax “immunoescaped”</th>
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CONCLUSIONS

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- Lower levels of FOXP3+ TILs induced by vaccination are maintained also along long-term treatment.

- Immune escape upon vaccine-induced immune response in our setting may be due not only to reduced immune recognition (lower Ag processing/presentation) but also to changes in the pattern of Ags expressed by tumor cells which may occur along vaccination.
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DISCLOSURE INFORMATION

Massimo Guidoboni, MD

The following relationships exist related to this presentation:

No Relationships to Disclose