ISTITUTO SCIENTIFICO ROMAGNOLO PER LO STUDIO E LA CURA DEI TUMORI

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

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Vaccination with dendritic cells loaded with autologous tumor lysate: clinical update of a phase II study in metastatic melanoma (Ridolfi et al. Melanoma Res 2011).

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

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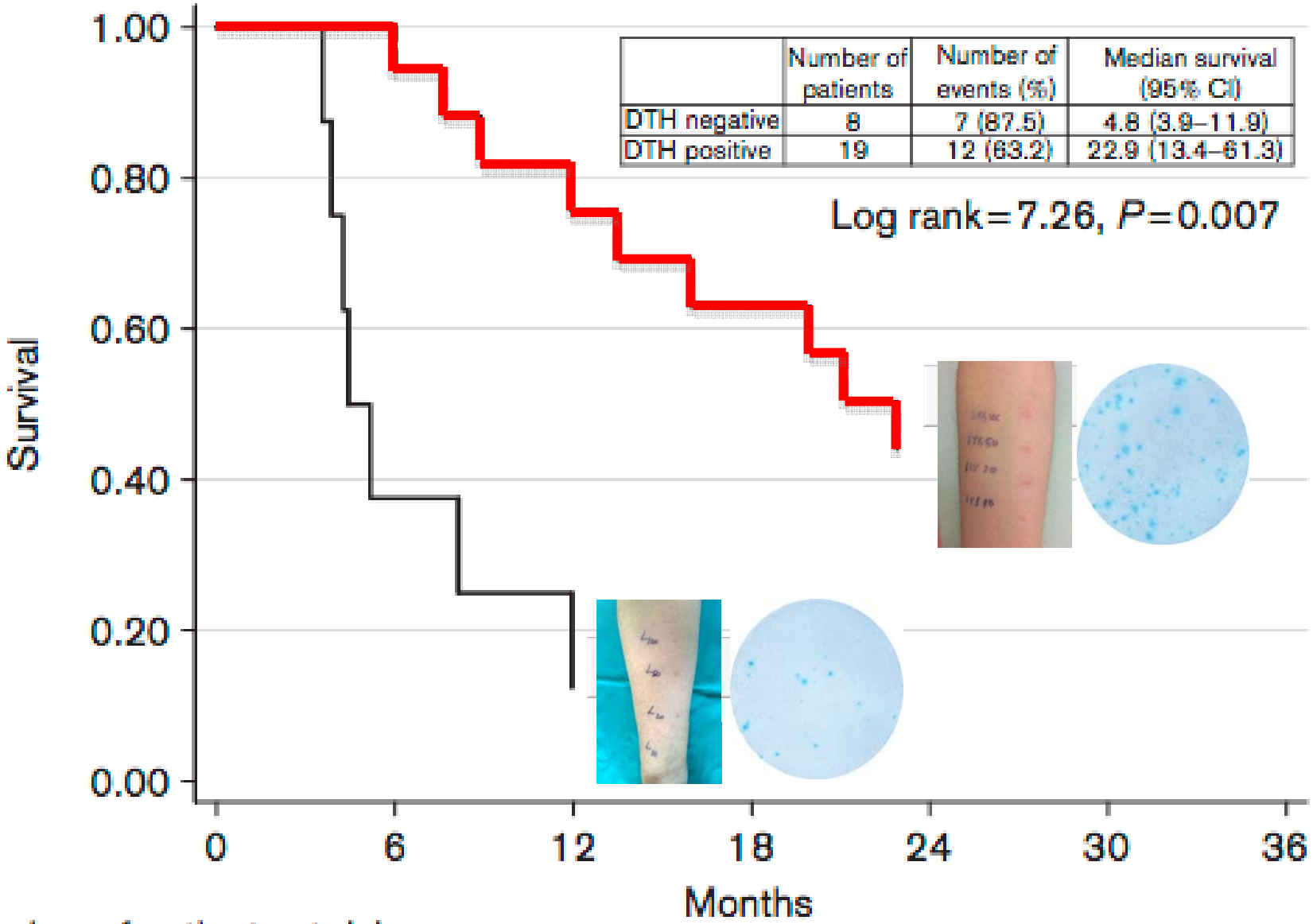
All clinical responders were also immunological responders (positive DTH to KLH and autologous tumor lysate and/or positive ELISPOT).



	Number of patients	Number of events (%)	Median survival (95% CI)
DTH negative	8	7 (87.5)	4.8 (3.9–11.9)
DTH positive	19	12 (63.2)	22.9 (13.4–61.3)

Number of patients at risk

DTH Neg	8	3	1	1	1	1	1
DTH Pos	19	18	12	10	7	7	5

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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)

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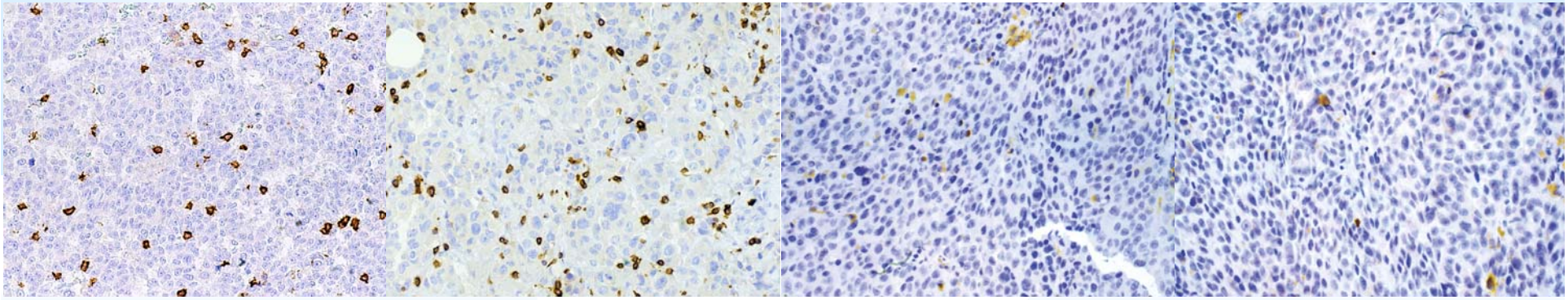
Immunohistochemistry for:



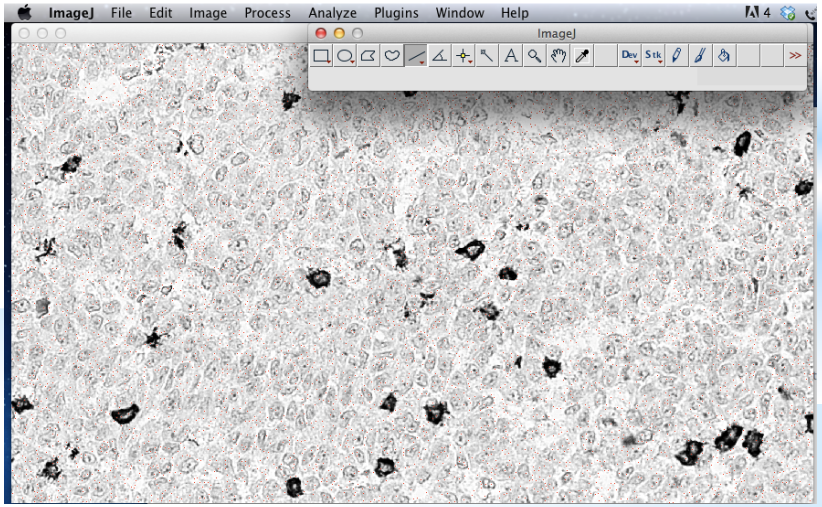
CD3 *CD8* *Granzyme B* *FOXP3*

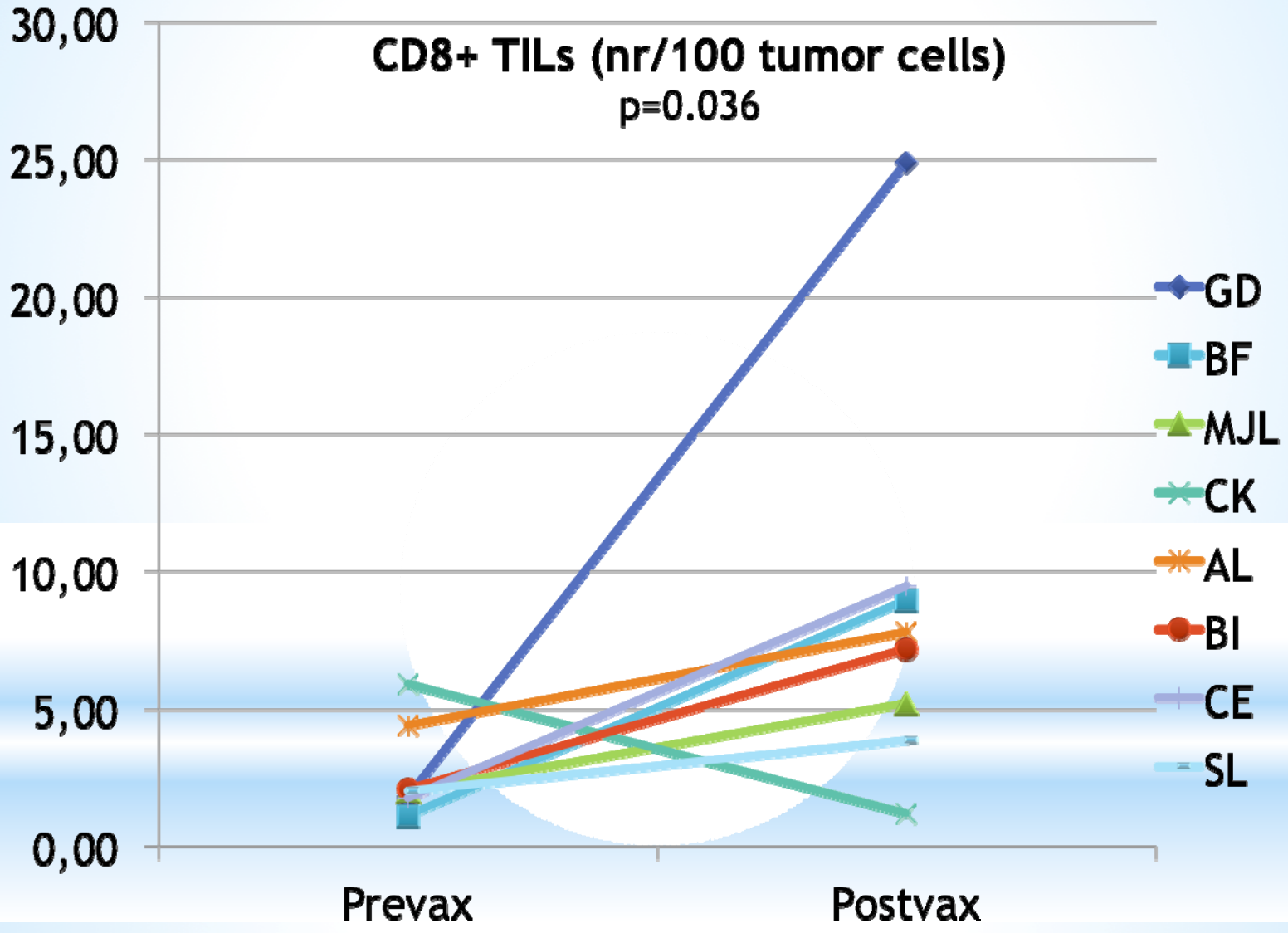
Digital camera acquisition

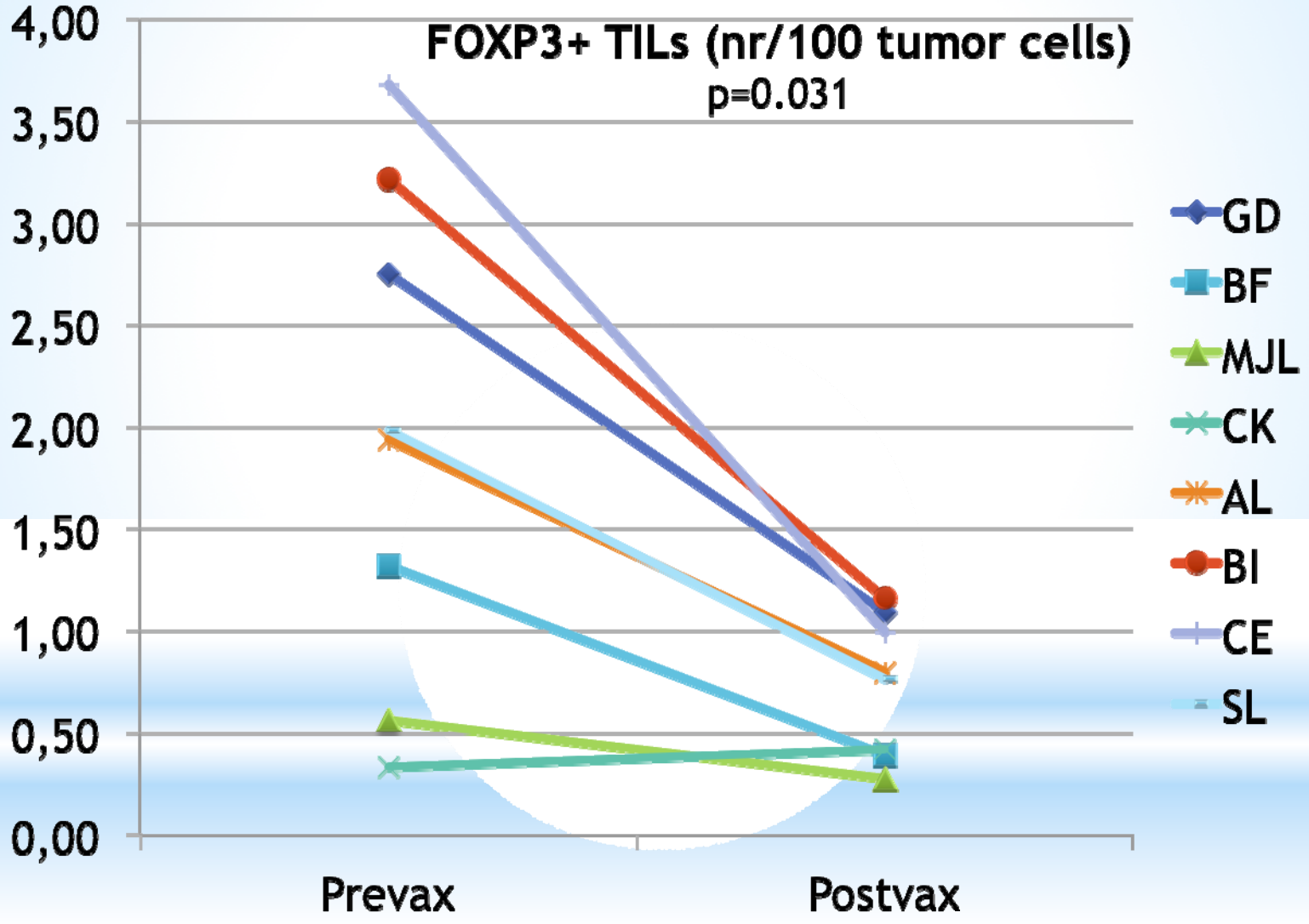
Computer-assisted counting

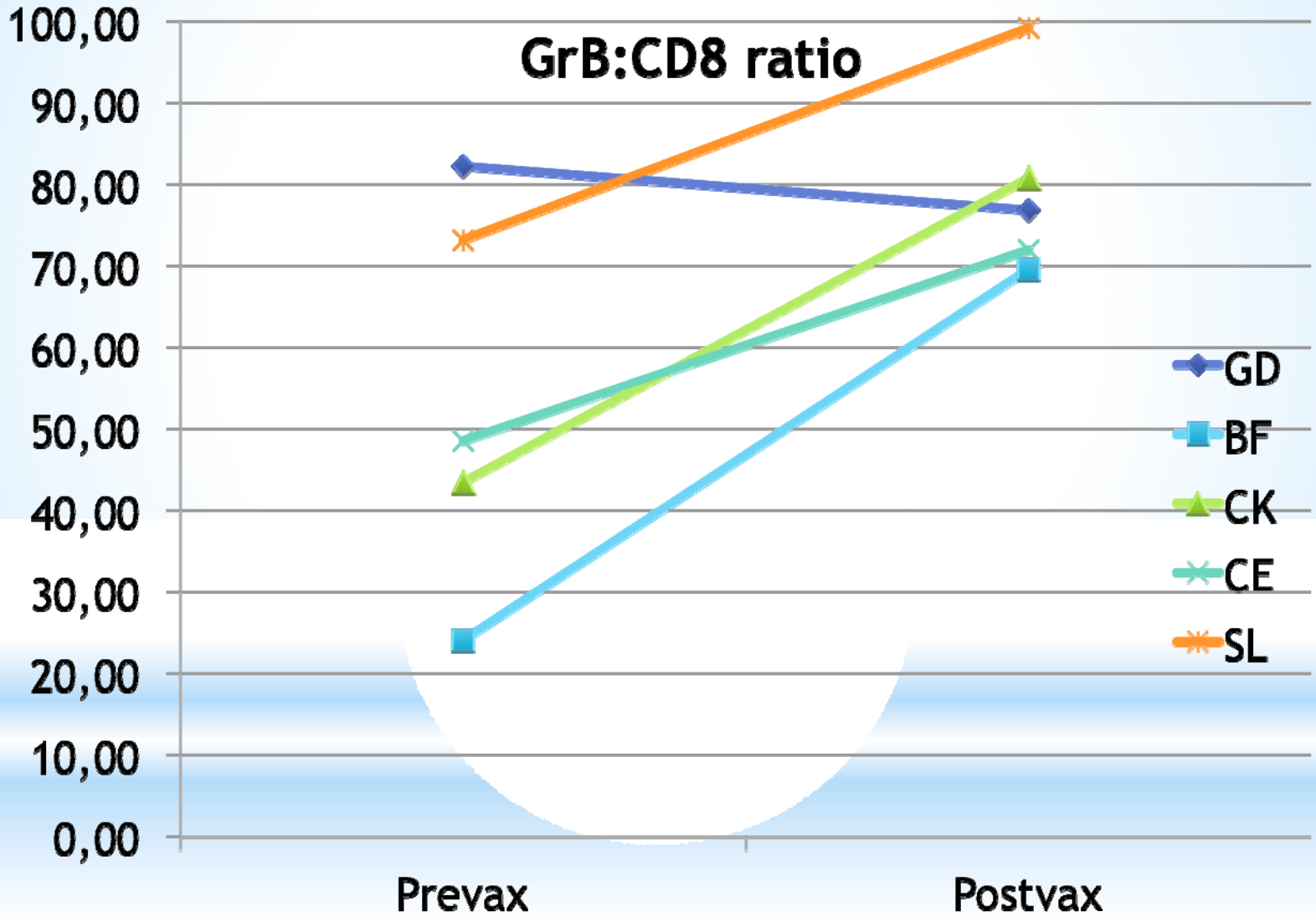
ImageJ
Image Processing and Analysis in Java

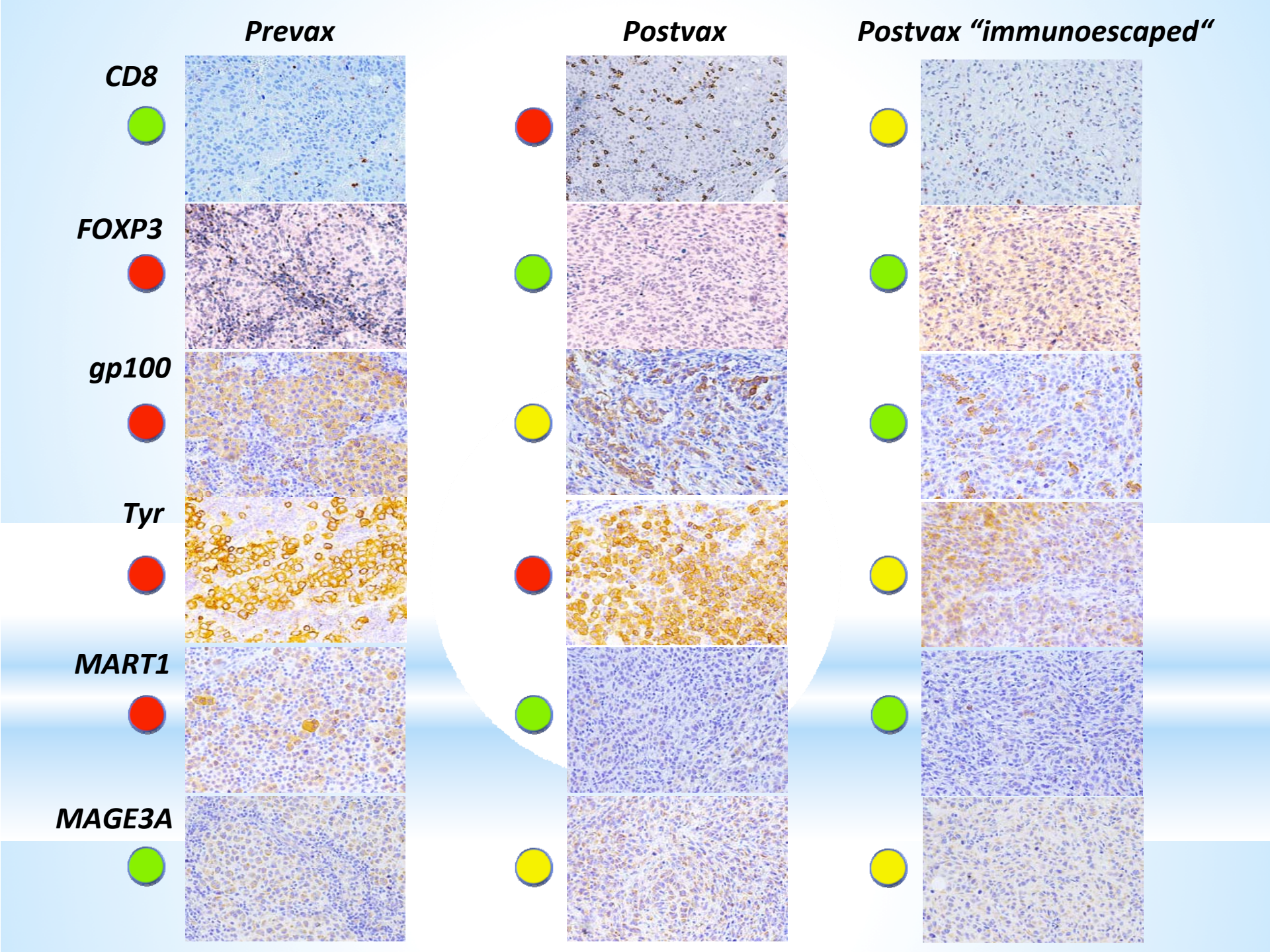
RSB Research Services Branch
National Institute of Mental Health
National Institute of Neurological Disorders and Stroke




CD8+ TILs (nr/100 tumor cells)
p=0.036
30,00
25,00
20,00
15,00
10,00
5,00
0,00
Prevax
Postvax
GD
BF
MJL
CK
AL
BI
CE
SL


FOXP3+ TILs (nr/100 tumor cells)
p=0.031
4,00
3,50
3,00
2,50
2,00
1,50
1,00
0,50
0,00
Prevax
Postvax
GD
BF
MJL
CK
AL
BI
CE
SL


GrB:CD8 ratio
100,00
90,00
80,00
70,00
60,00
50,00
40,00
30,00
20,00
10,00
0,00
Prevax
Postvax
GD
BF
CK
CE
SL


Prevax
Postvax
Postvax "immunoescaped"
CD8
FOXP3
gp100
Tyr
MART1
MAGE3A

CONCLUSIONS

-In immunoresponsive advanced melanoma patients DC vaccination induces strong CTL responses at tumor sites.

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- DC vaccination might "relief" immunosuppression in tumor microenvironment by reducing FOXP3+ regulatory TILs.
- Reduced immunosuppression is likely functionally relevant (higher cytotoxic activation of CD8+ CTLs).
- 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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FASTER
BH 2006

DISCLOSURE INFORMATION

Massimo Guidoboni, MD

The following relationships exist related to this presentation:

No Relationships to Disclose