

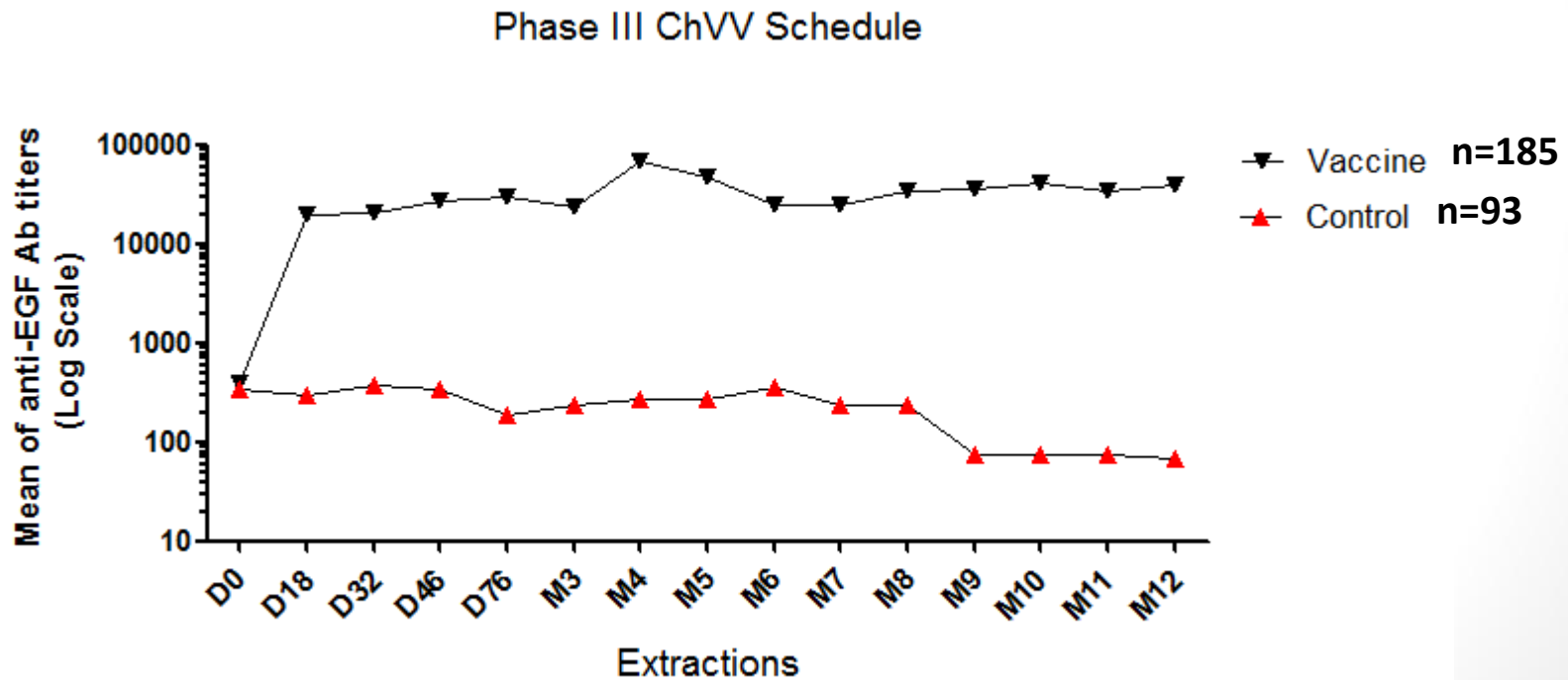
4th Global Meeting EGF Vaccine

Phase III ChVV Schedule: Immune Response Analysis

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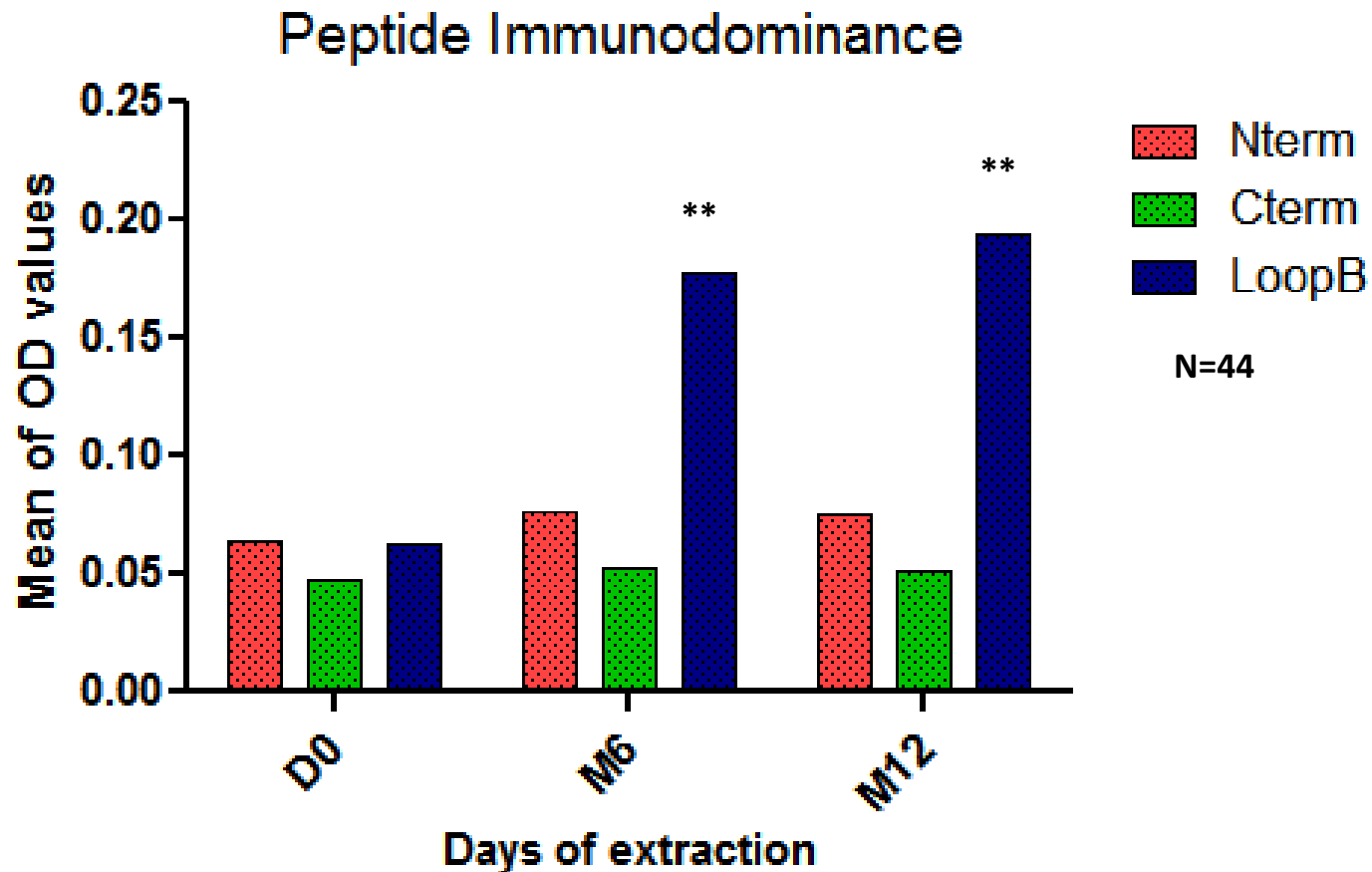
Kinetics of Ab Titers

Anti-EGF Ab titers were significantly greater in vaccinated patients.



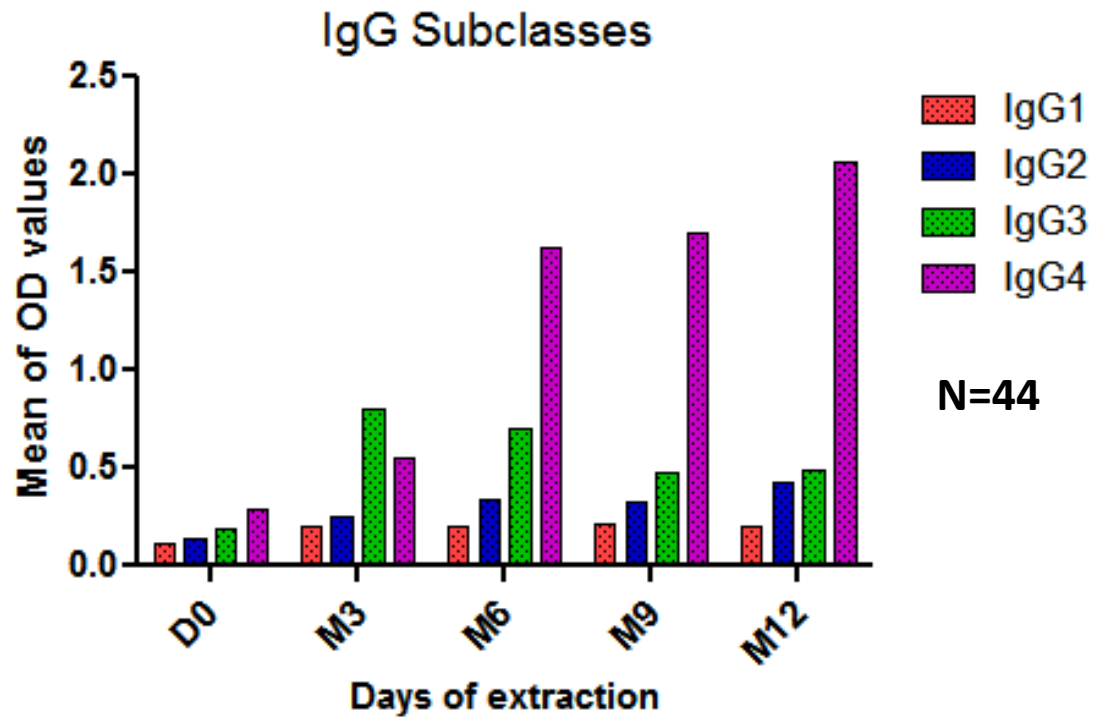
Peptide Immunodominance

The c antibody response is directed toward the central EGF/EGFR binding region (Loop B) in 46% of the evaluated patients

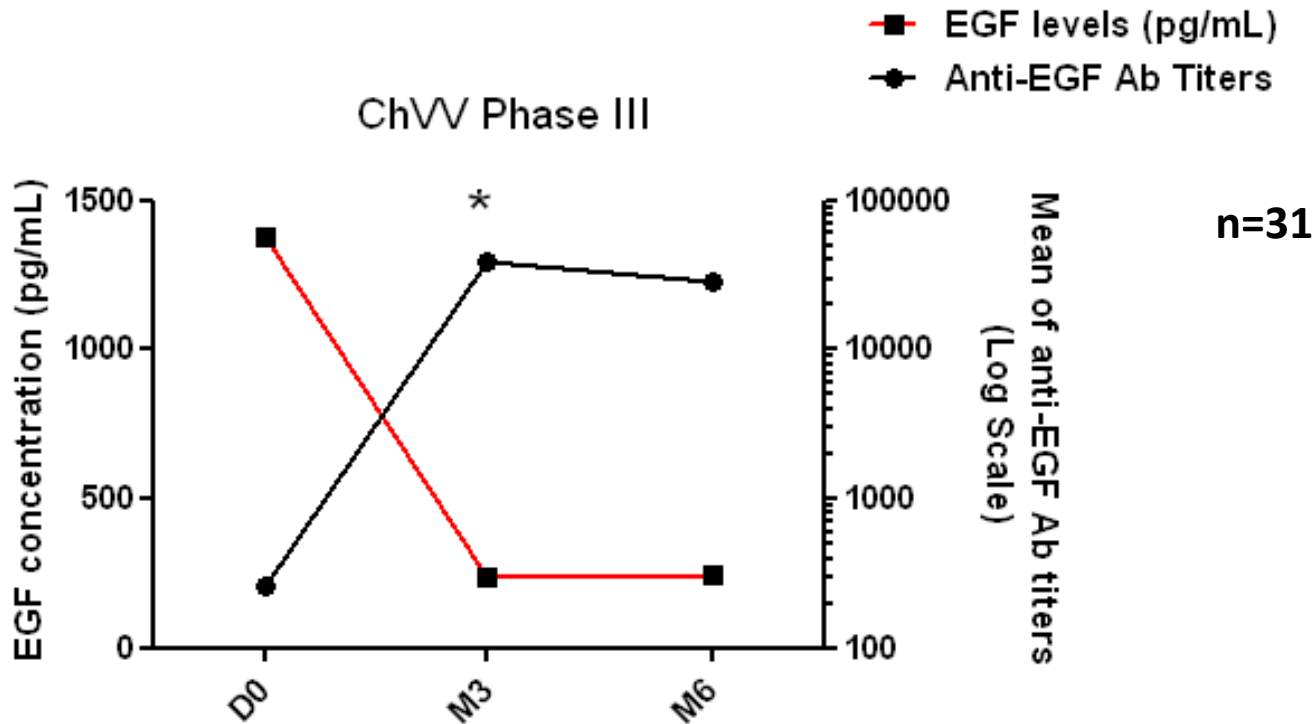


IgG Subclasses

The predominant IgG subclasses are IgG3 and IgG4



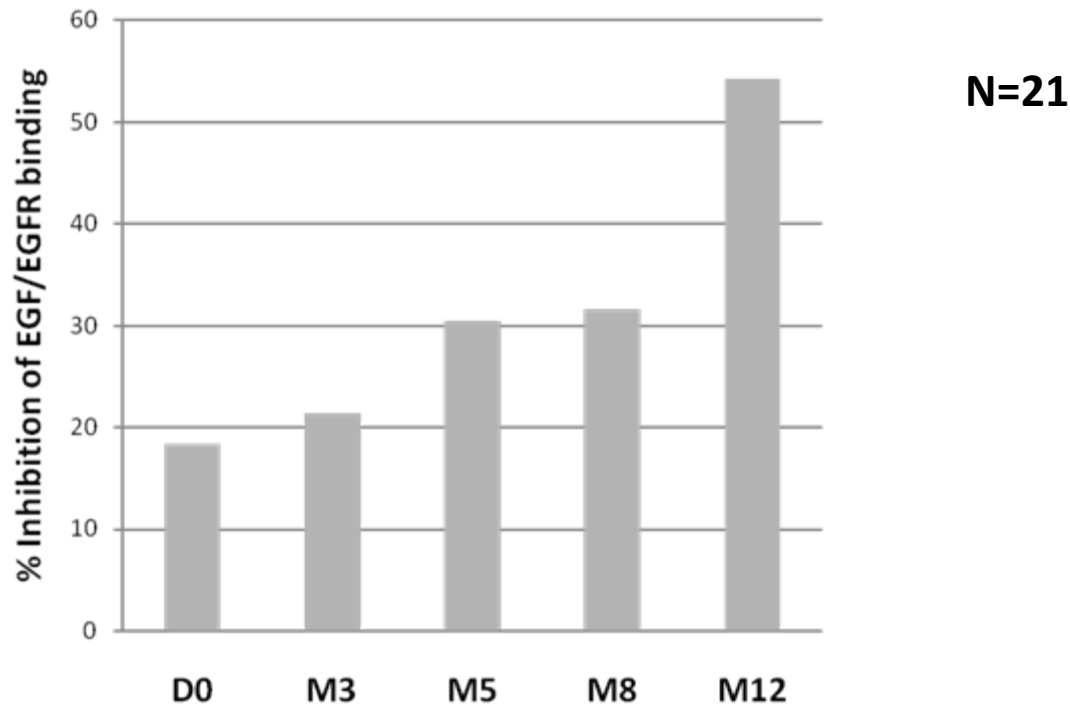
Ab Titers & EGF Levels



There is an inverse correlation between antibody titers and the levels of EGF in serum

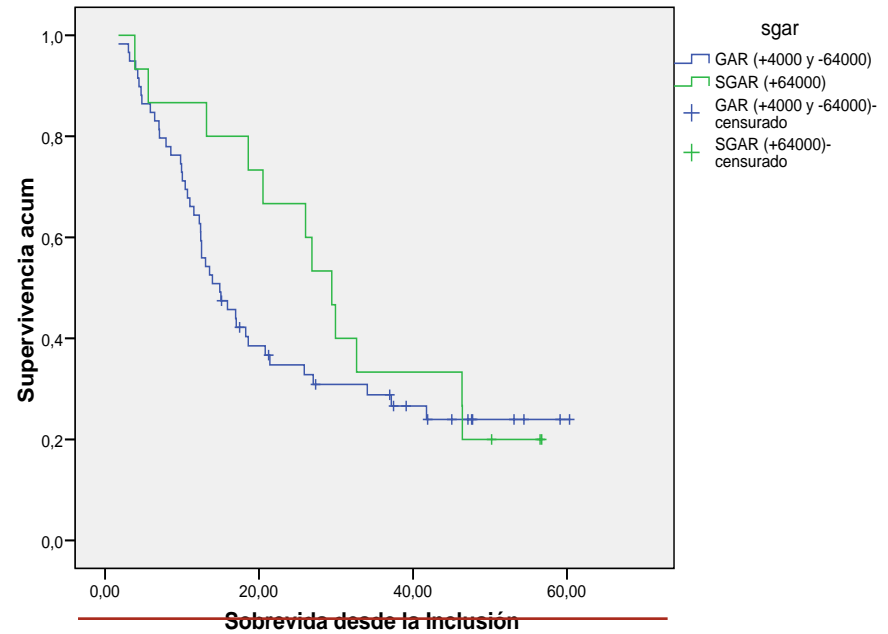
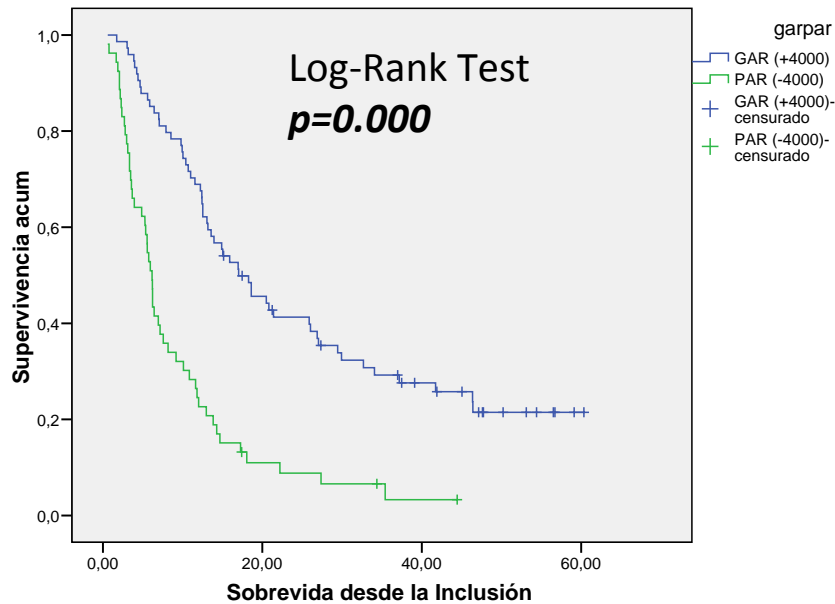
Biological activity of generated Abs

The EGF-specific antibodies generated after immunization are able to inhibit the EGF/EGFR binding



Immune Response & Clinical Outcome

There is a correlation between survival and the magnitude of the antibody response generated after immunization



	(months)	(months)
PAR (N=53)	9.53	6.16
GAR (N=74)	26.28	17.03

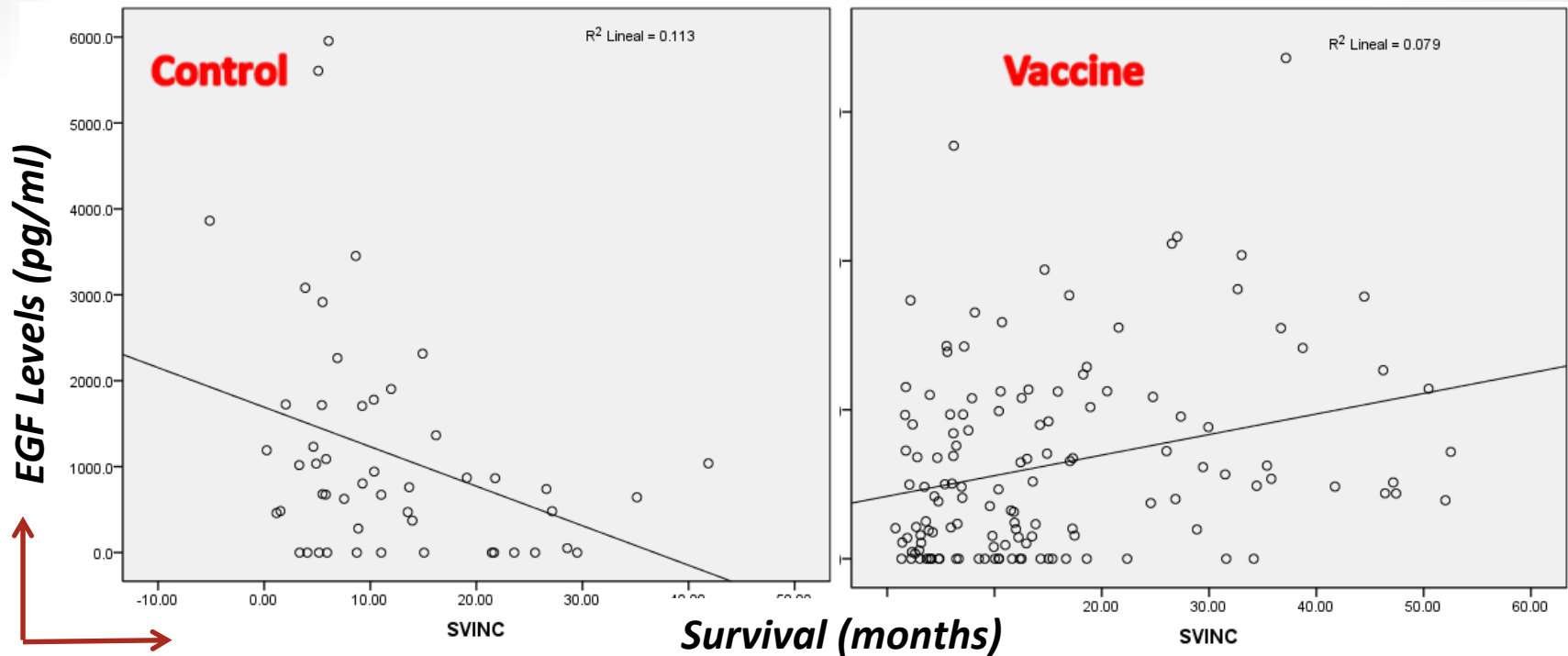
	Mean (months)	Median (months)
GAR (N=59)	25.18	14.9
SGAR (N=15)	31.03	29.4

PAR (poor antibody responder (Ab titer <4000))

GAR (good antibody responder (Ab titer >4000, 4X seroconversion))

SGAR (super good antibody responder (Ab titer >64000, 4X seroconversion))

EGF levels as a predictive factor of treatment benefit



p=0.001

Mean: 1186 pg/ml

N: 49

p=0.018

Mean: 1185 pg/ml

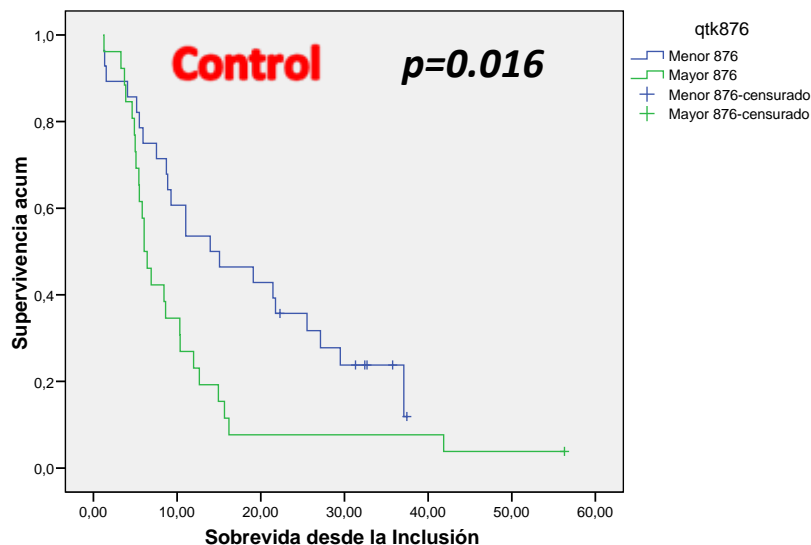
N: 133

There are a correlation between serum EGF levels before treatment and survival in both groups.

EGF levels as a predictive factor of treatment benefit

The EGF levels before treatment can predict the benefit of patients from EGF-P64k vaccination

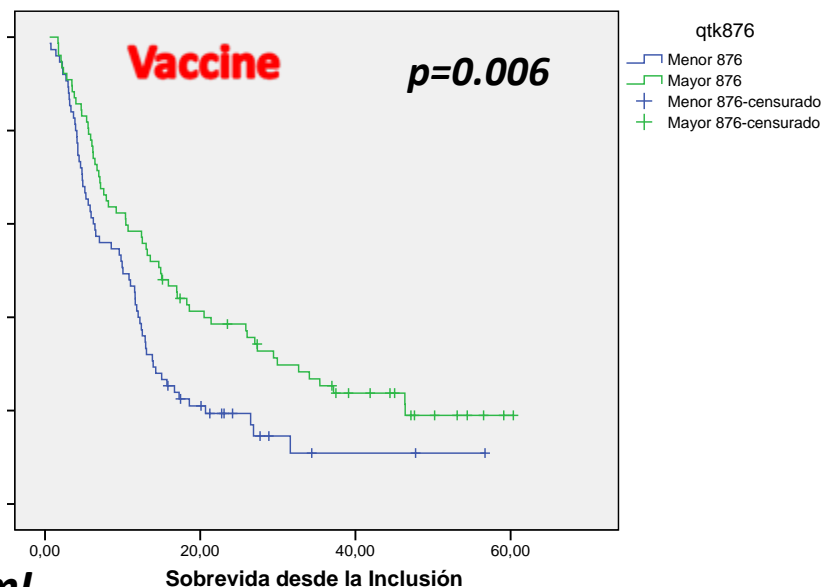
Funciones de supervivencia



Median: 876 pg/mL

Control	Mean (months)	Median (months)
>876 (N=26)	10.8	6.06
<876 (N=28)	18.2	13.9

Funciones de supervivencia



Vaccine	Mean (months)	Median (months)
>876 (N=77)	23.67	14.09
<876 (N=75)	15.19	10.03

Concluding remarks

- **The immunization with EGF generates a greater antibody response in vaccinated patients.**
 - **The EGF-specific antibody response is mainly of IgG3 and IgG4 subclass in all evaluated patients.**
 - **The EGF-specific antibody response is mainly directed toward the central EGF/EGFR binding region (LoopB) in a subset of patients.**
- **There is an inverse correlation between antibody titers and the levels of EGF in serum.**
- **The EGF immunization generates specific antibodies able to inhibit EGF/EGFR binding.**
 - **A greater antibody response is associated with a better survival.**
- **Serum EGF levels before treatment can predict the benefit of patients from EGF immunotherapy.**

Ongoing & Future Experiments

Ongoing Experiments

- Determination of the inhibition of EGFR activation by patients sera.
- Determination of affinity maturation of the IgG response by Biacore Technology.

Future Experiments

- Determination of Th response pattern by Luminex.
- Determination of the specific cellular immune response by ELISPOT.

Acknowledgments

Patients

Center of Molecular Immunology

Clinical Immunology Department

Zuyen Castillo Tech.

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Amnely Gonzalez Tech.

Clinical Trials Department

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Camilo Rodriguez

Tania Crombet

Clinical Institutions

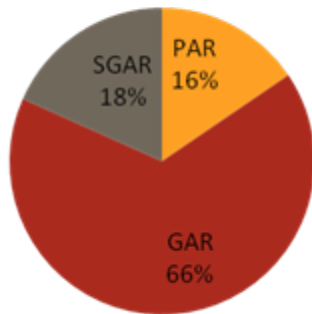
Clinical Researchers

Clinical Staff

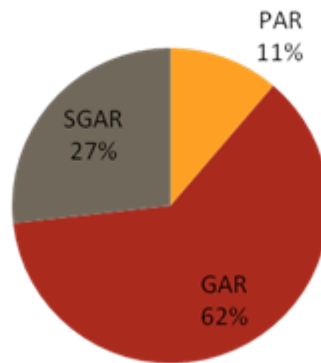
Gracias!!!

Thanks!!!

PhaseIII M3



PhaseIII M6



PhaseIII ChtVV

