

## Ensayo de citotoxicidad de CD19 humanizado con células ND317T

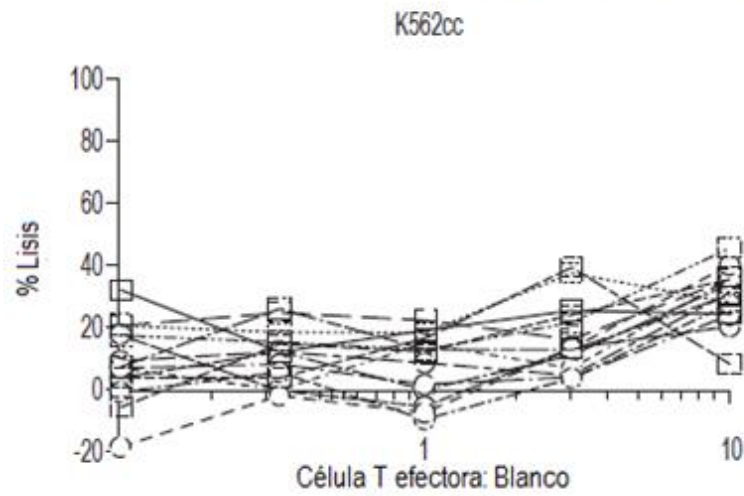


FIG. 1A

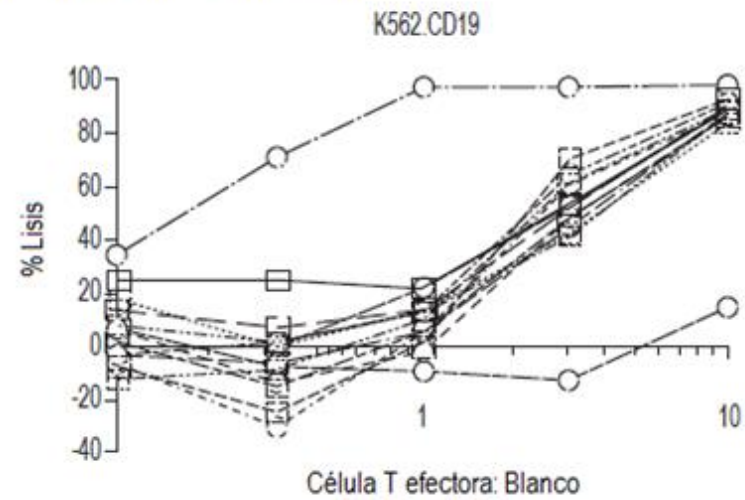


FIG. 1B

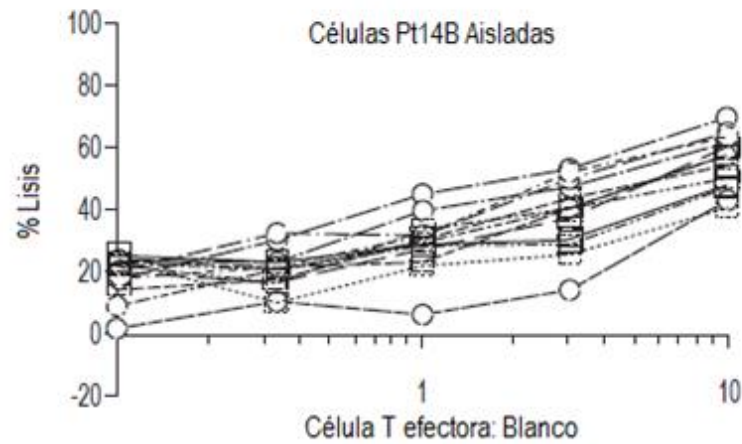
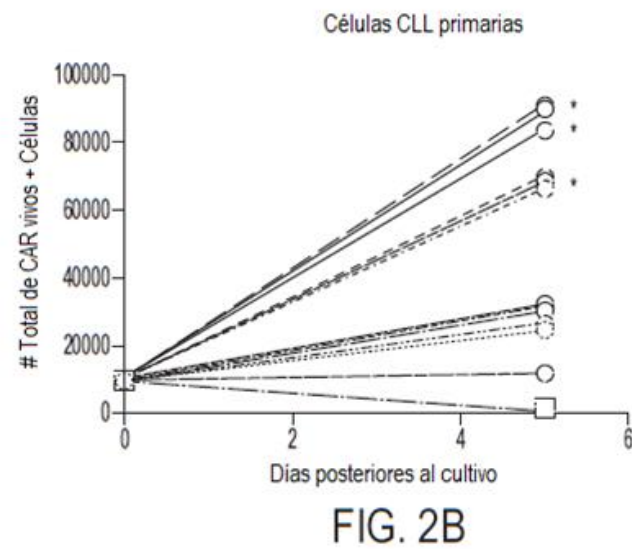
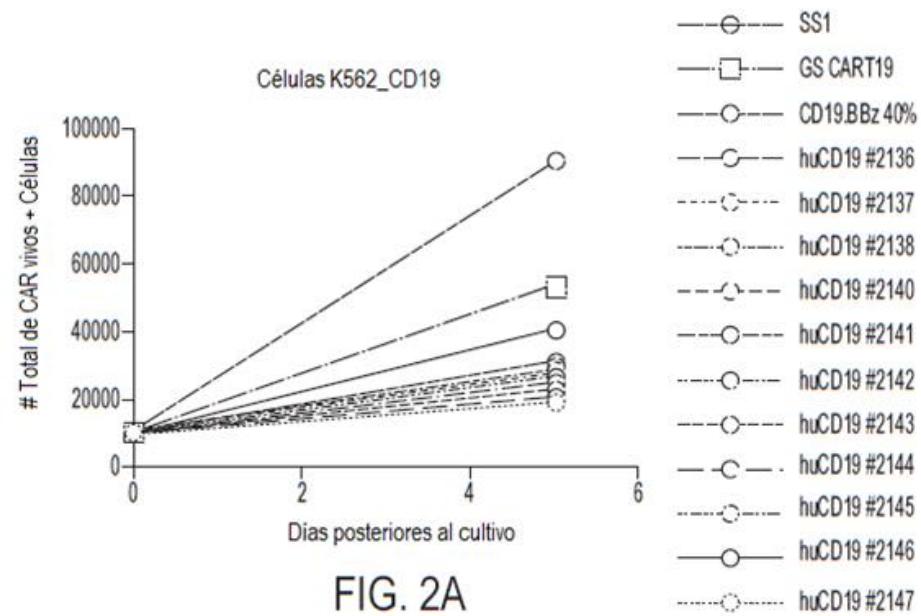


FIG. 1C

- SS1.BBz
- GS CART19
- CD19.BBz
- 2136
- 2137
- 2138
- 2140
- 2141
- 2142
- 2143
- 2144
- 2145
- 2146
- 2147



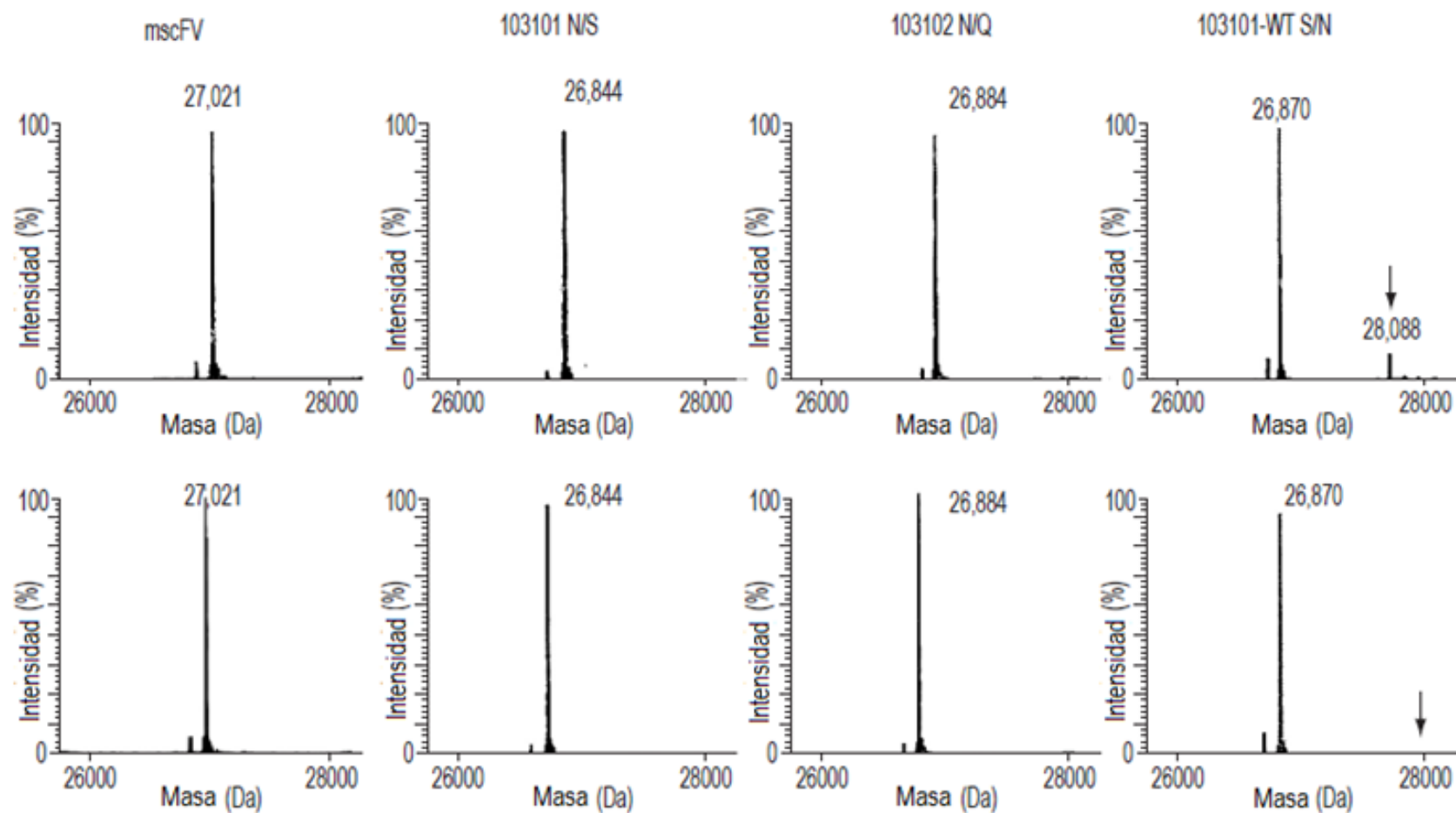


FIG. 3

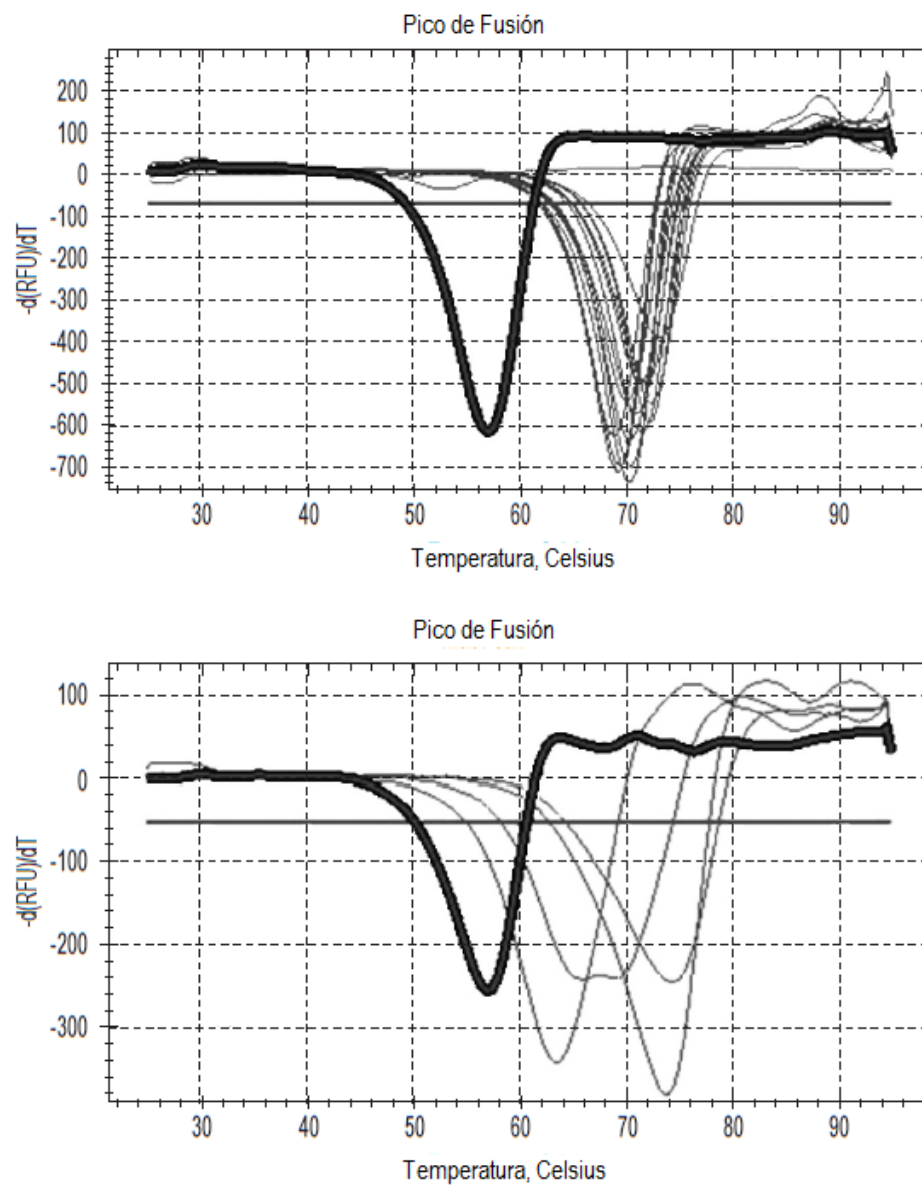


FIG. 4

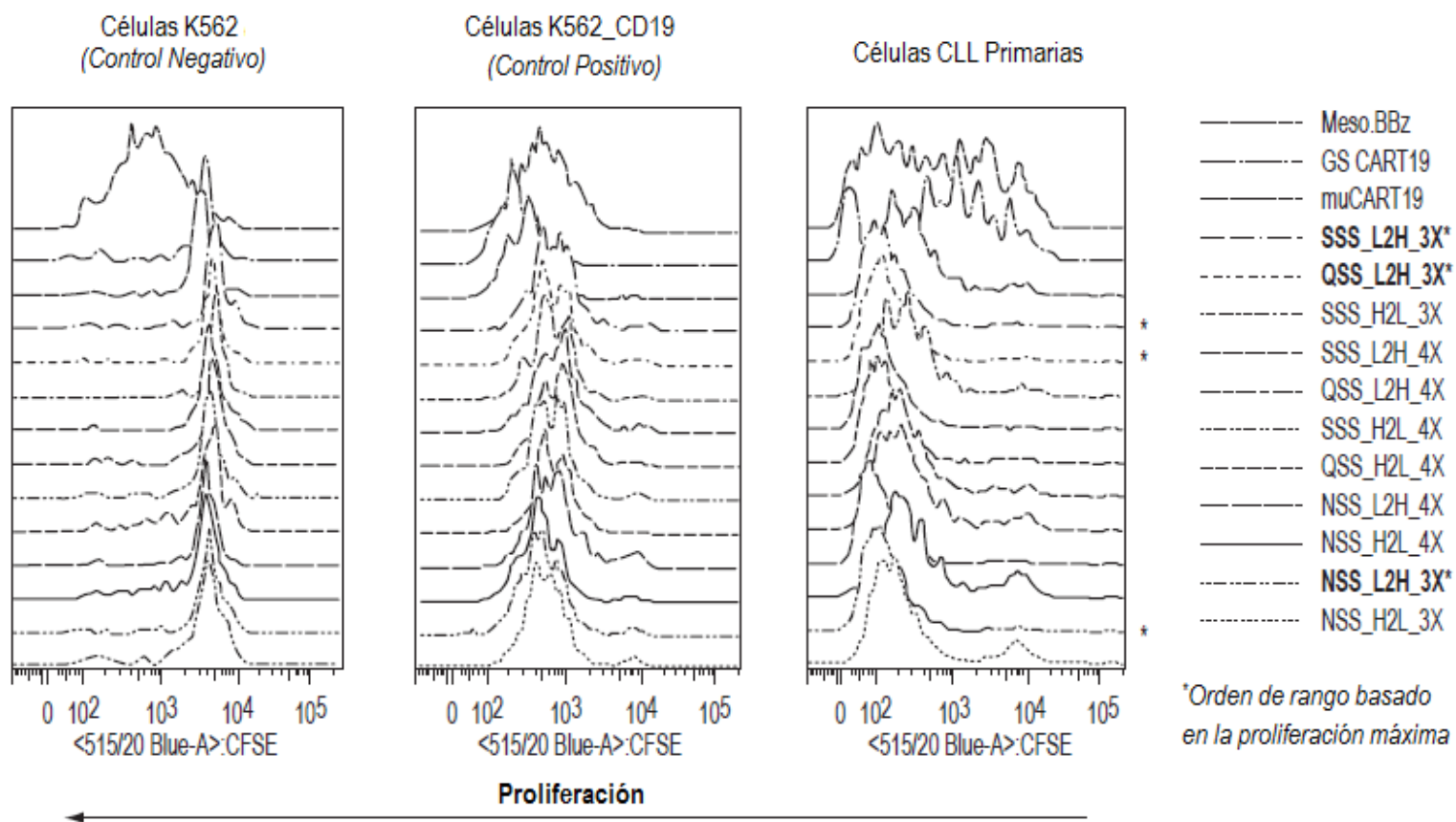


FIG. 5

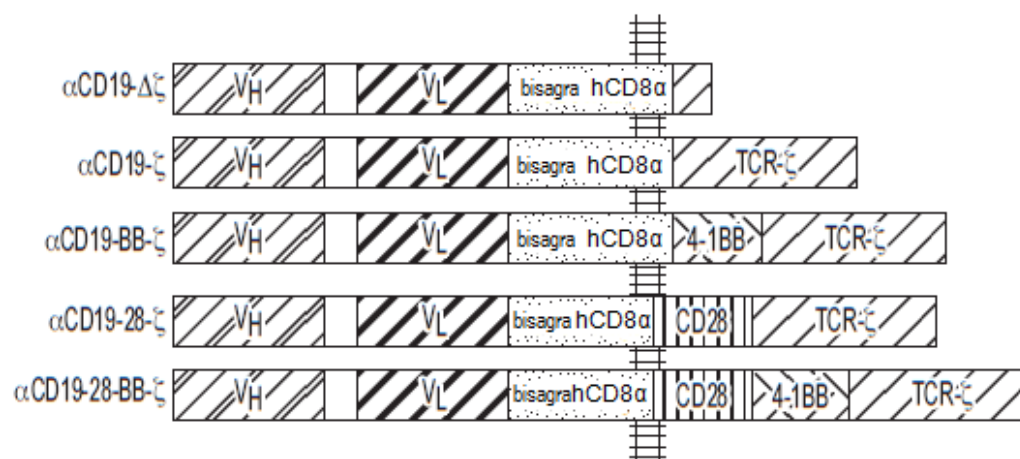


FIG. 6A

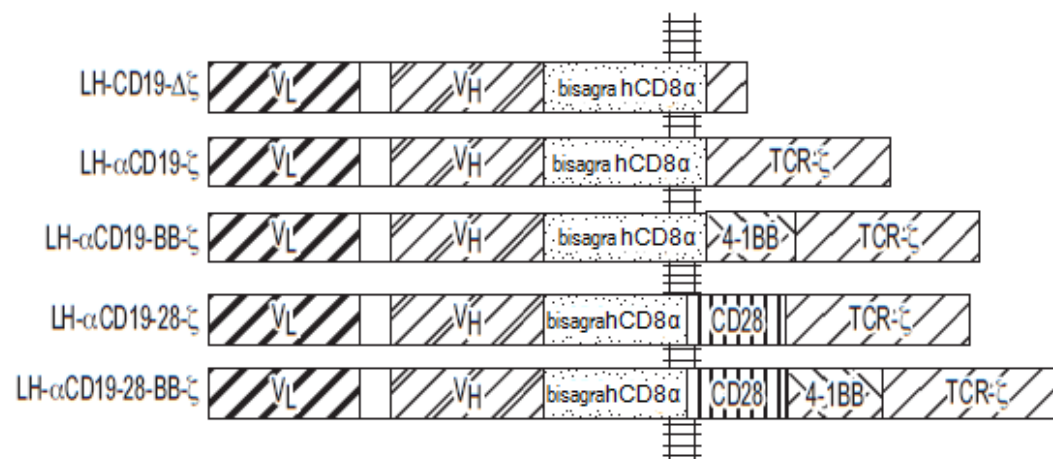


FIG. 6B

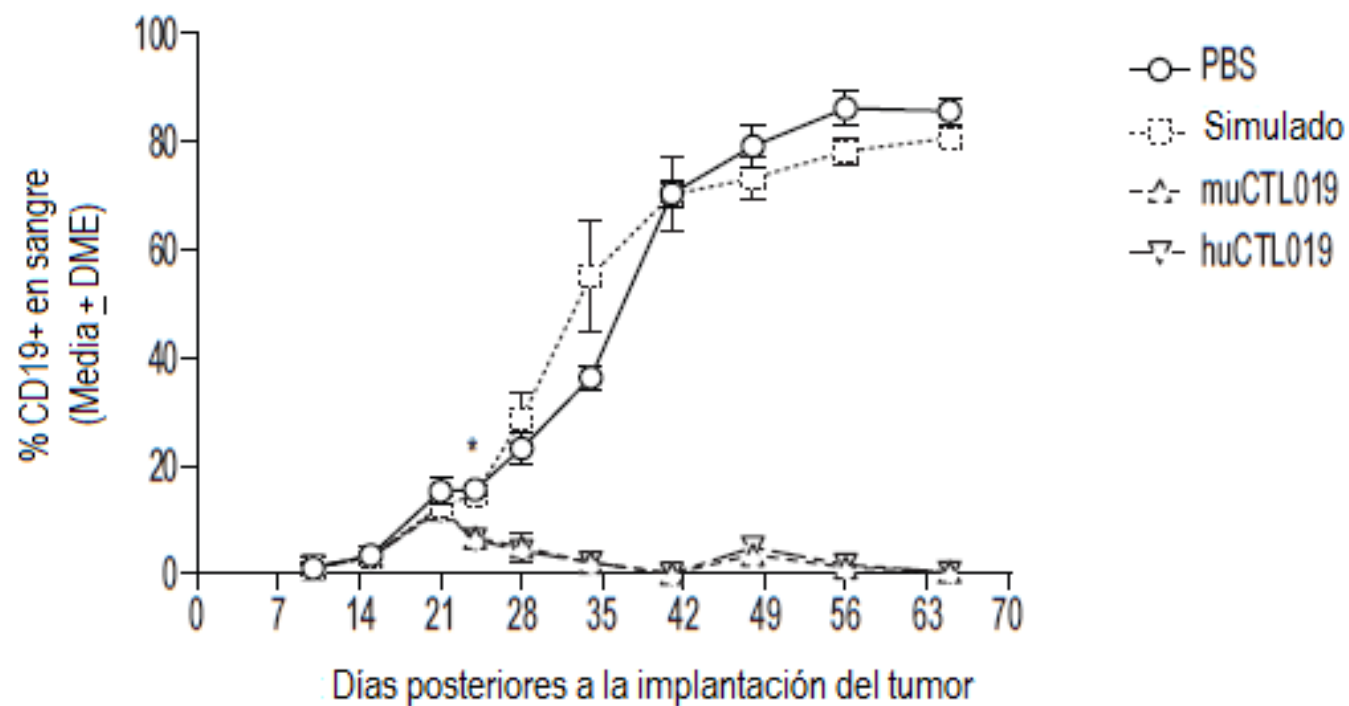
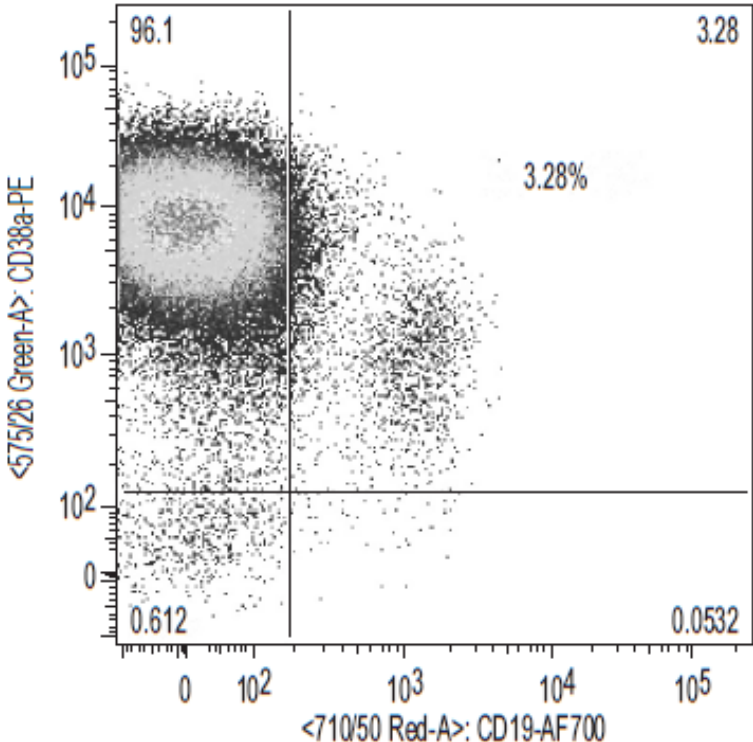


FIG. 7



células oscuras CD138+ CD45 tumorales teñidas para CD19 (eje x) y CD38 (eje y)

FIG. 8

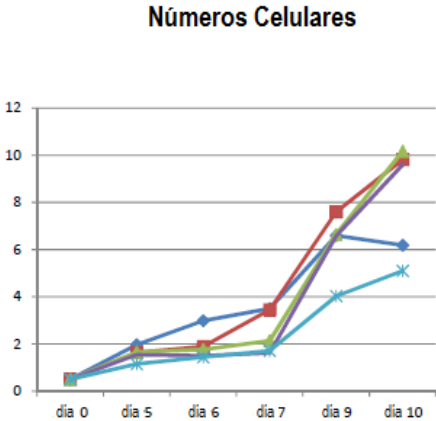


FIG. 9A

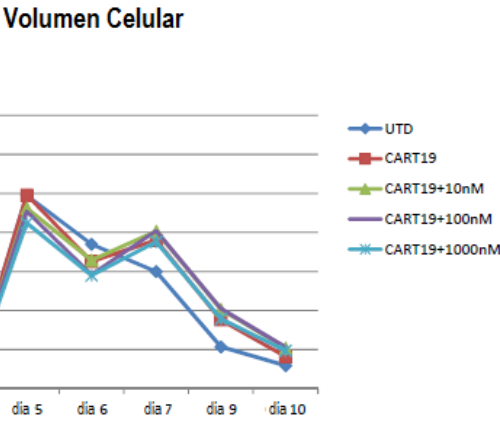
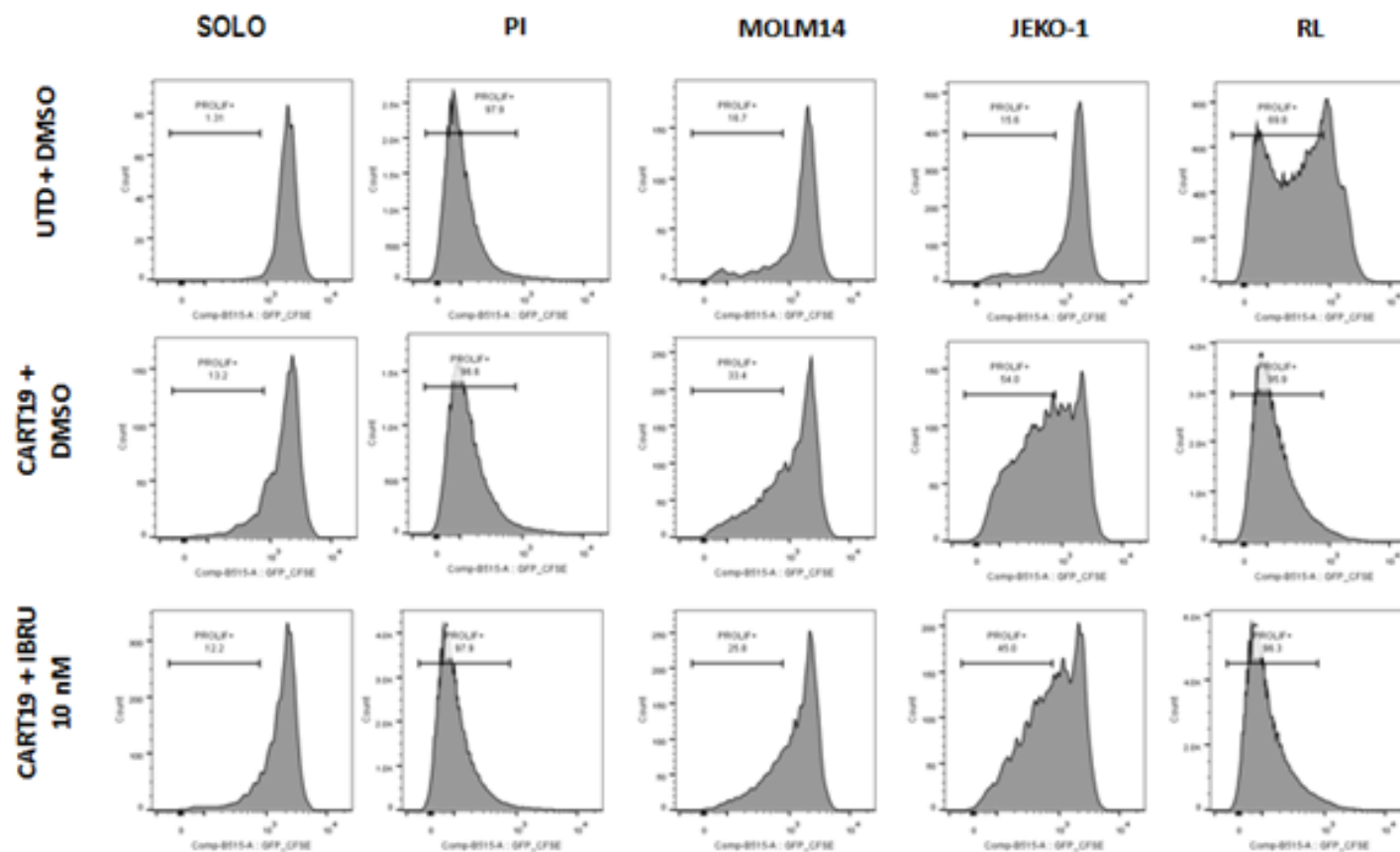


FIG. 9B

FIG. 10A

## ENSAYO DE PROLIFERACIÓN CELULAR DE CFSE DE 5 DÍAS



## ENSAYO DE PROLIFERACIÓN CELULAR DE CFSE DE 5 DÍAS

FIG. 10A CONT.

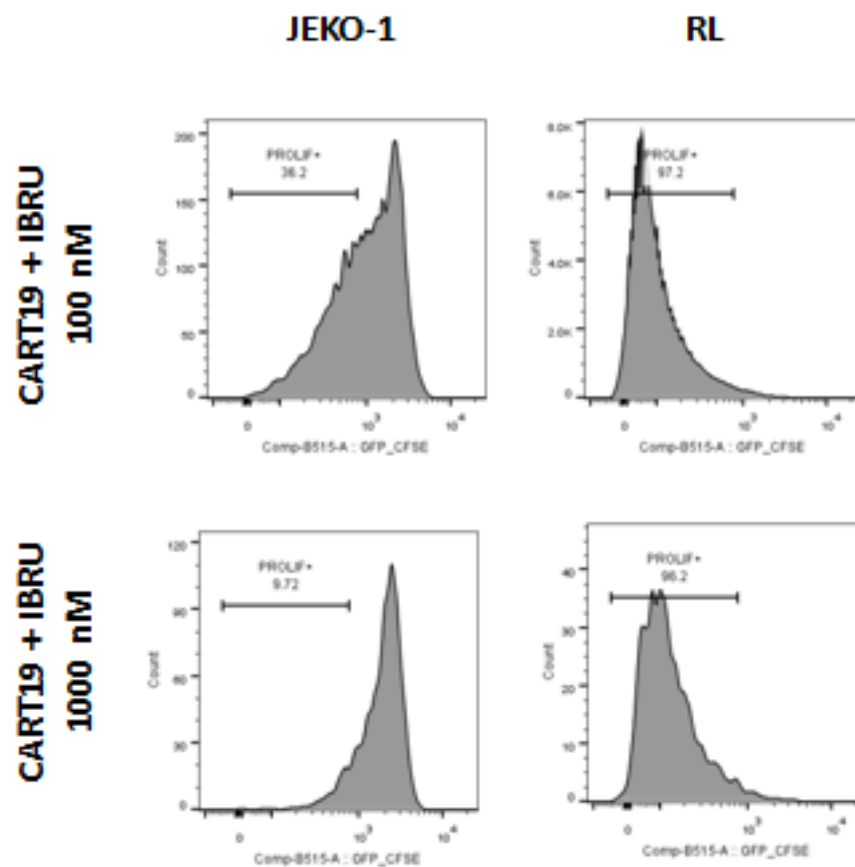


FIG. 10B

## ENSAYO DE PROLIFERACIÓN CELULAR DE CFSE DE 5 DÍAS

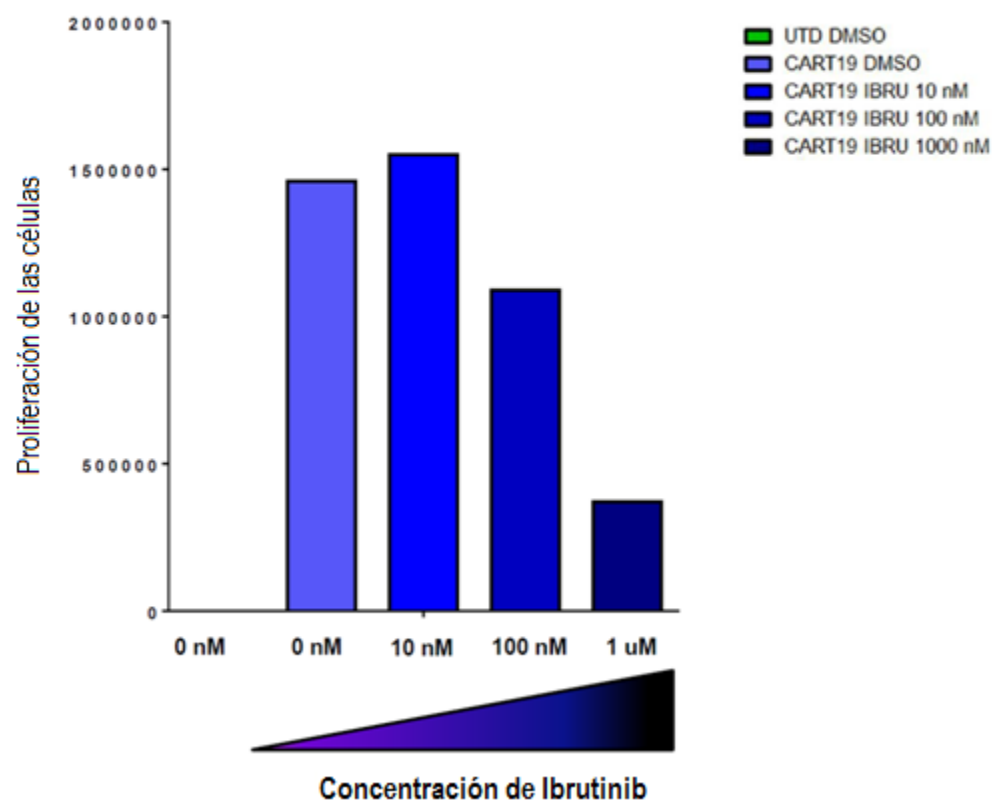


FIG. 11A

## DESGRANULACIÓN DE CD107a

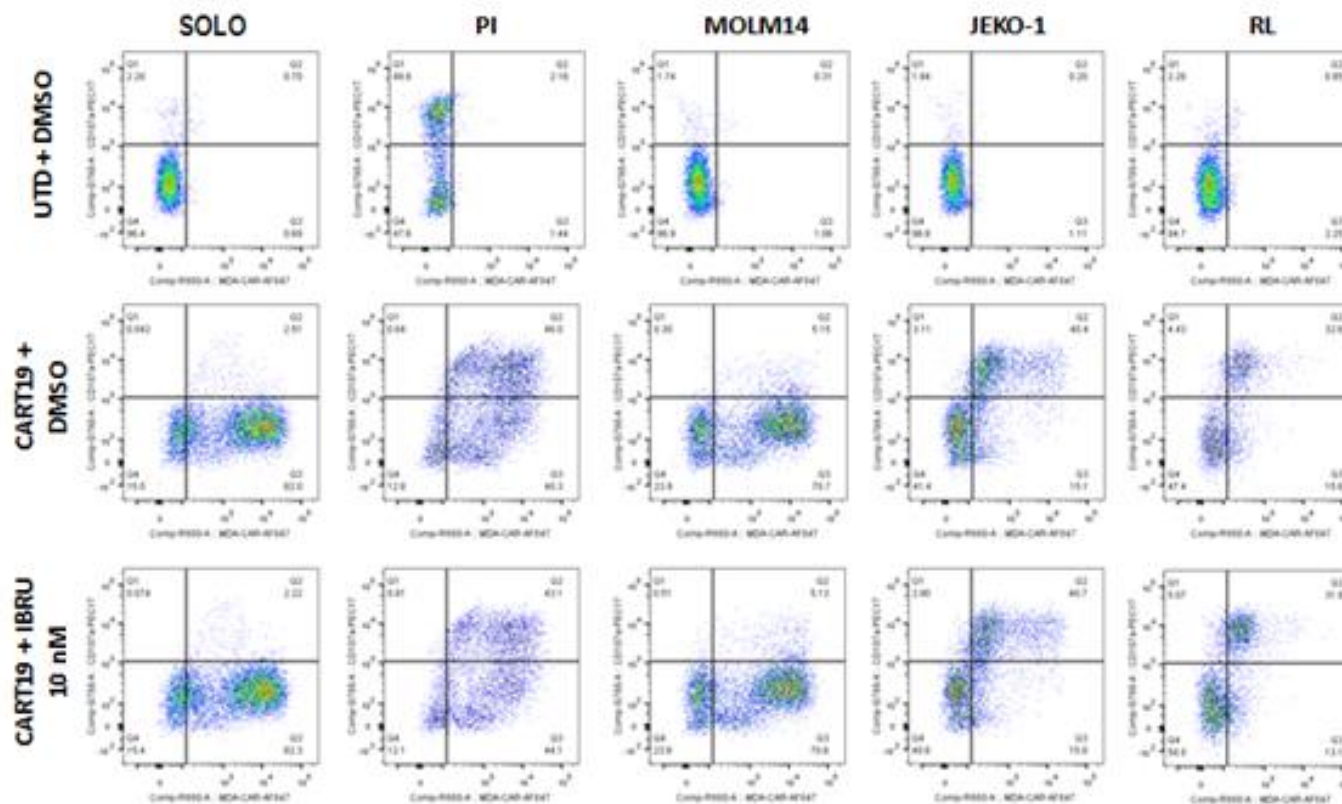


FIG. 11A CONT.

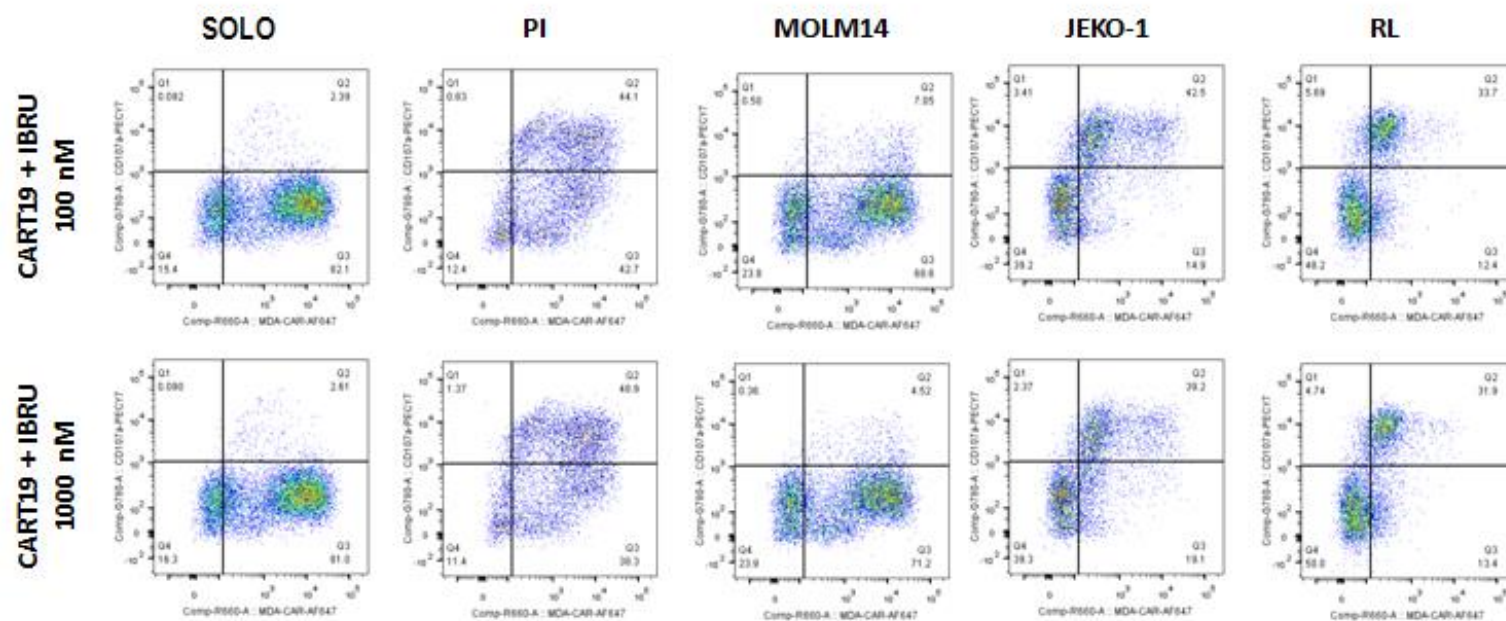
**DESGRANULACIÓN DE CD107a**

FIG. 11B

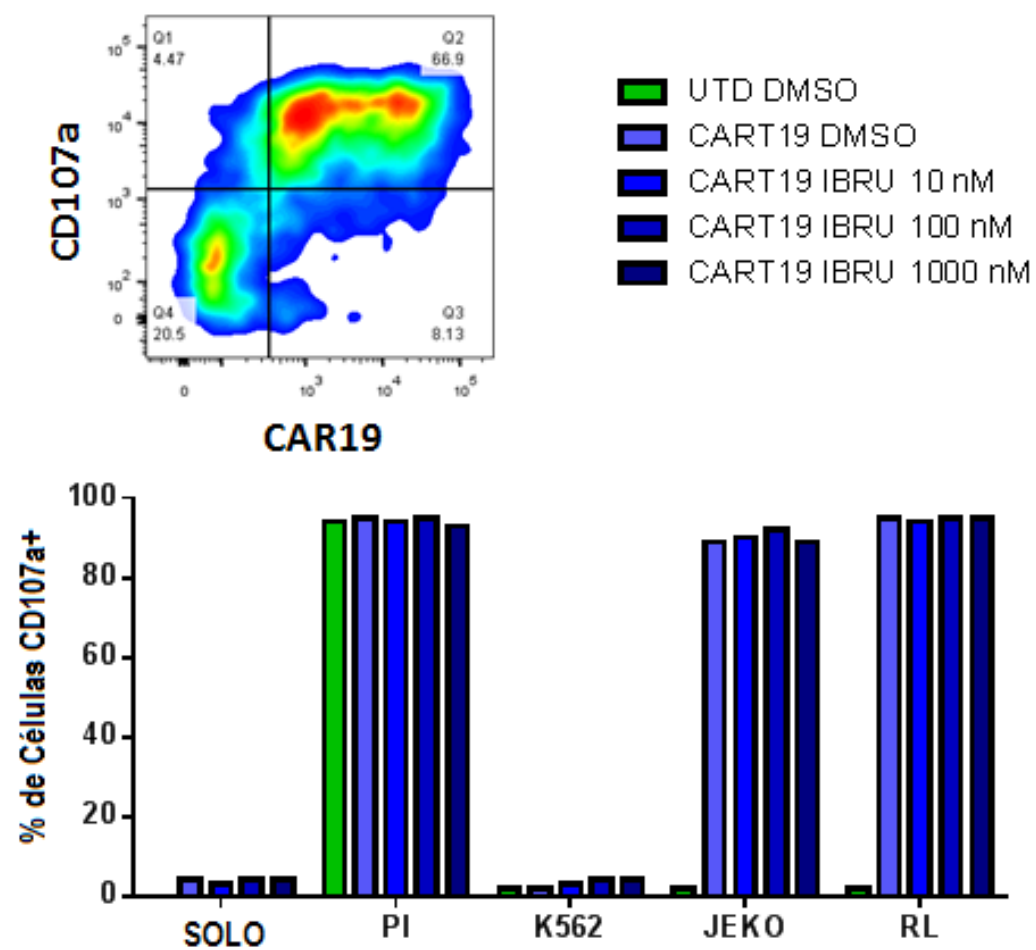


FIG. 12

## PRODUCCIÓN INTRA-CITOPLASMÁTICA DE IL-2

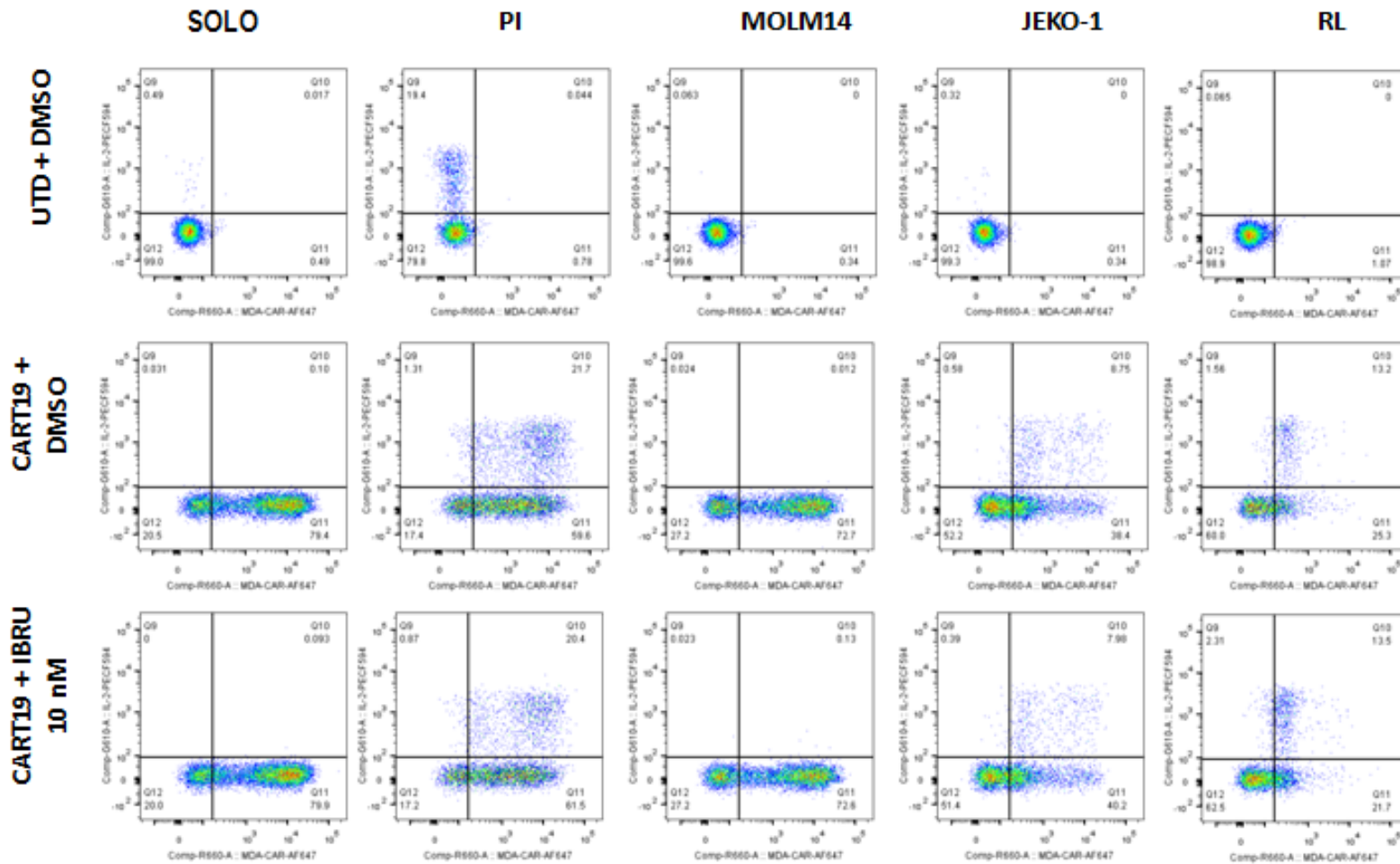


FIG. 12 CONT.

## PRODUCCIÓN INTRA-CITOPLASMÁTICA DE IL-2

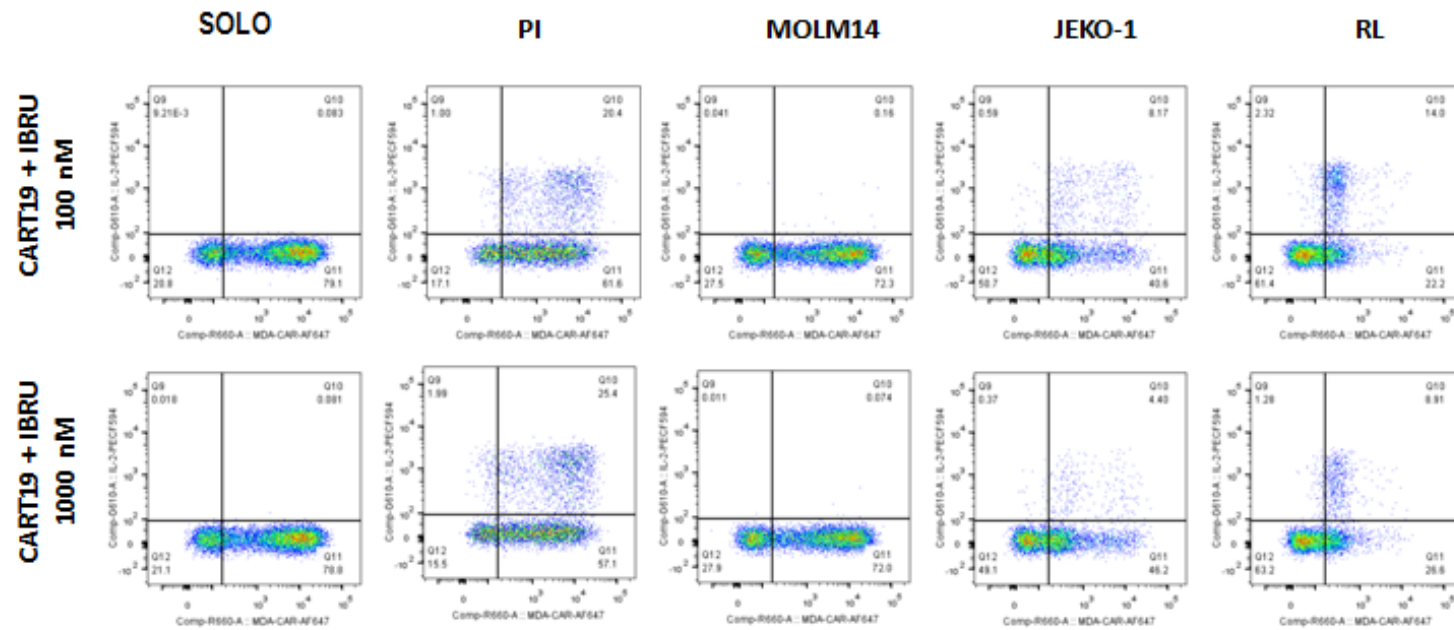


FIG. 13

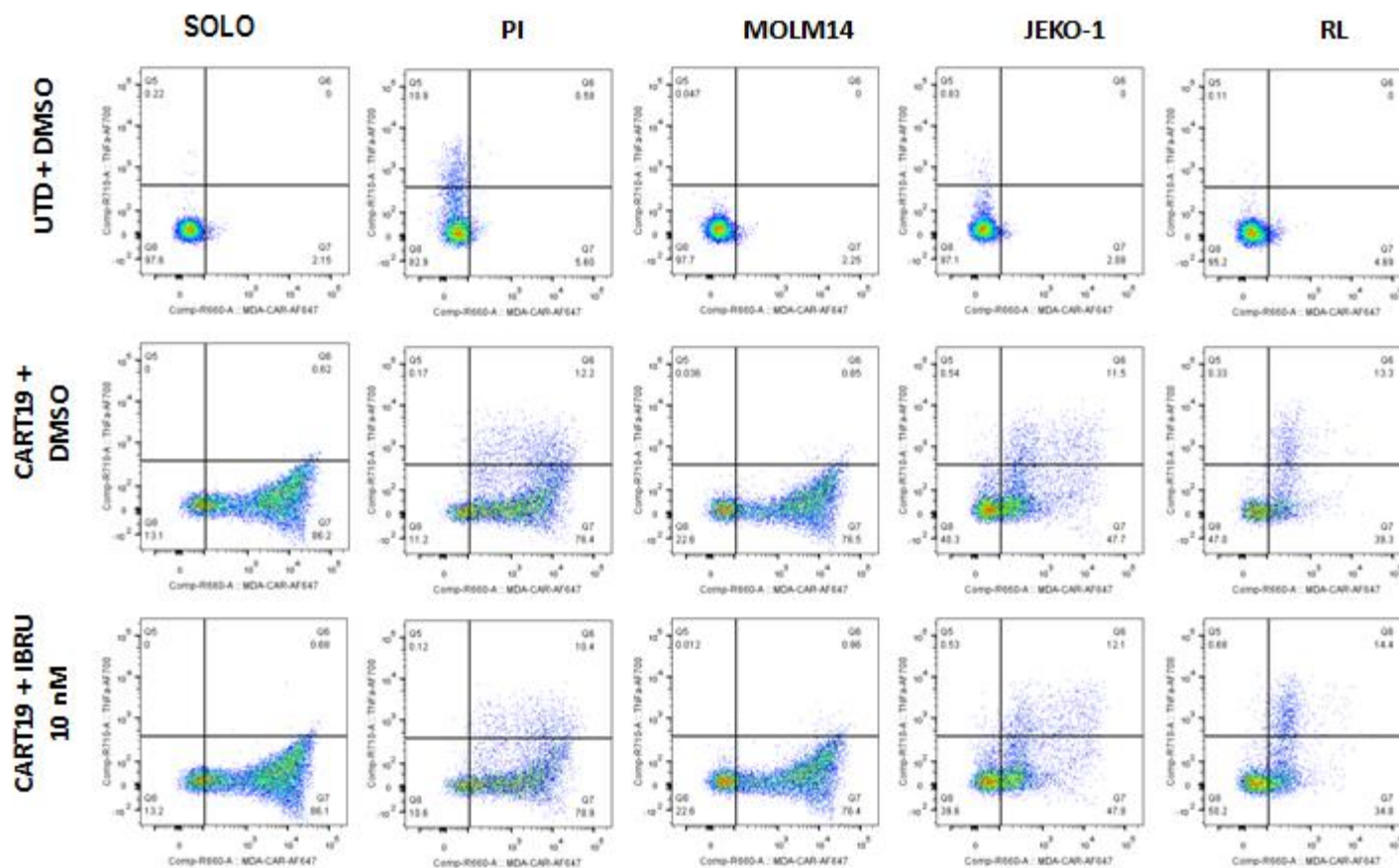
PRODUCCIÓN INTRA-CITOPLASMÁTICA DE **TNF $\alpha$** 

FIG. 13 CONT.

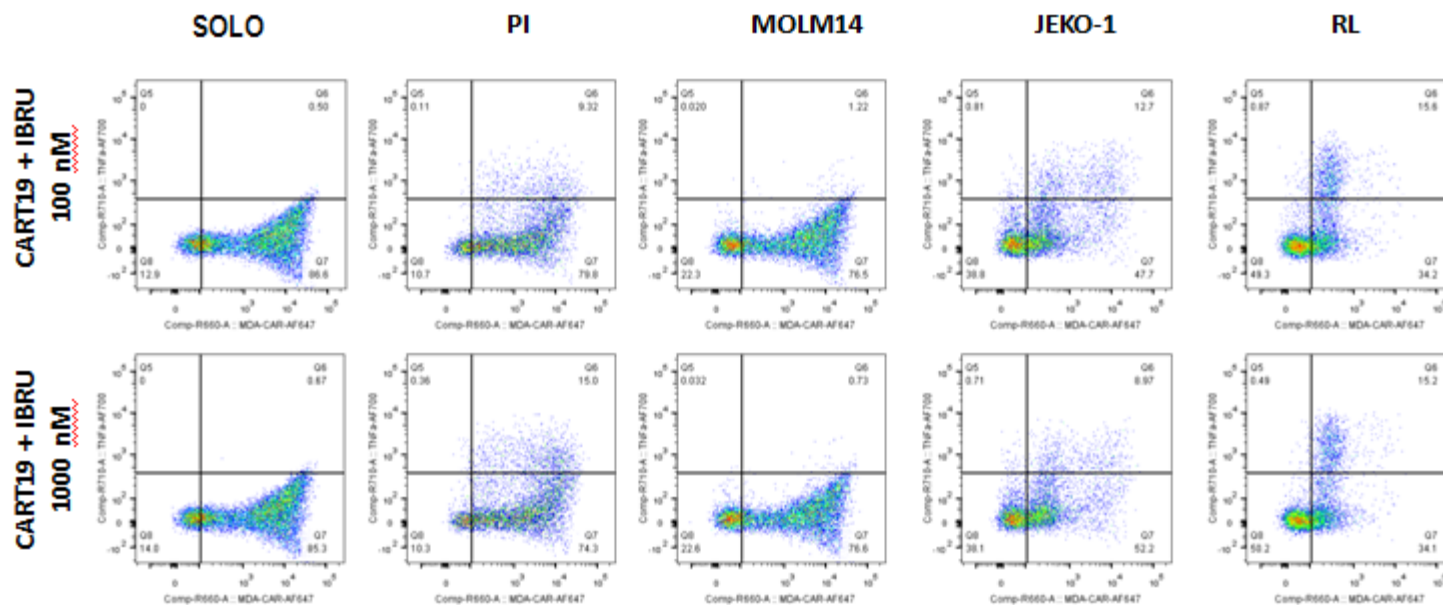
PRODUCCIÓN INTRA-CITOPLASMÁTICA DE **TNF $\alpha$** 

FIG. 14

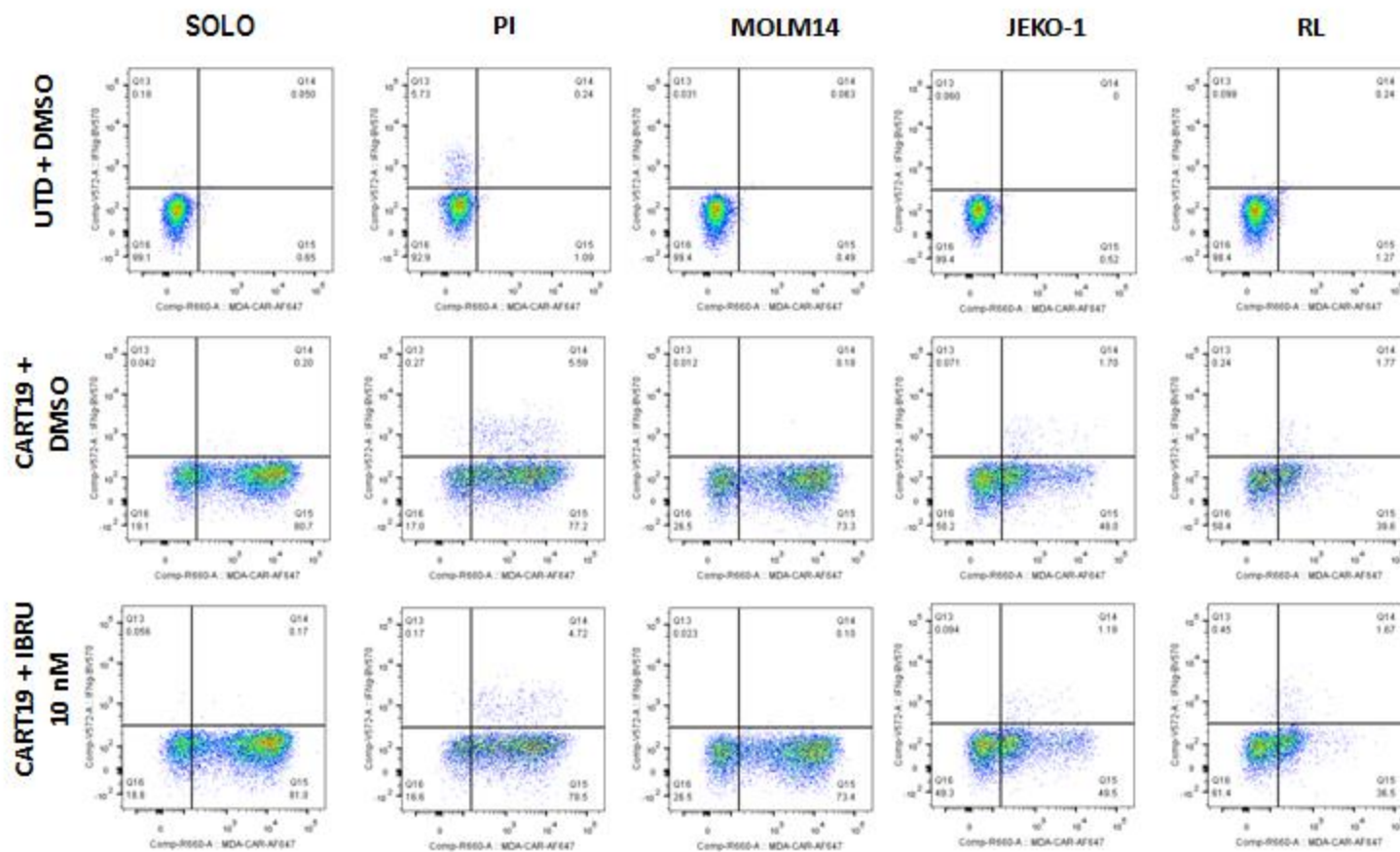
PRODUCCIÓN INTRA-CITOPLASMÁTICA DE IFN $\gamma$ 

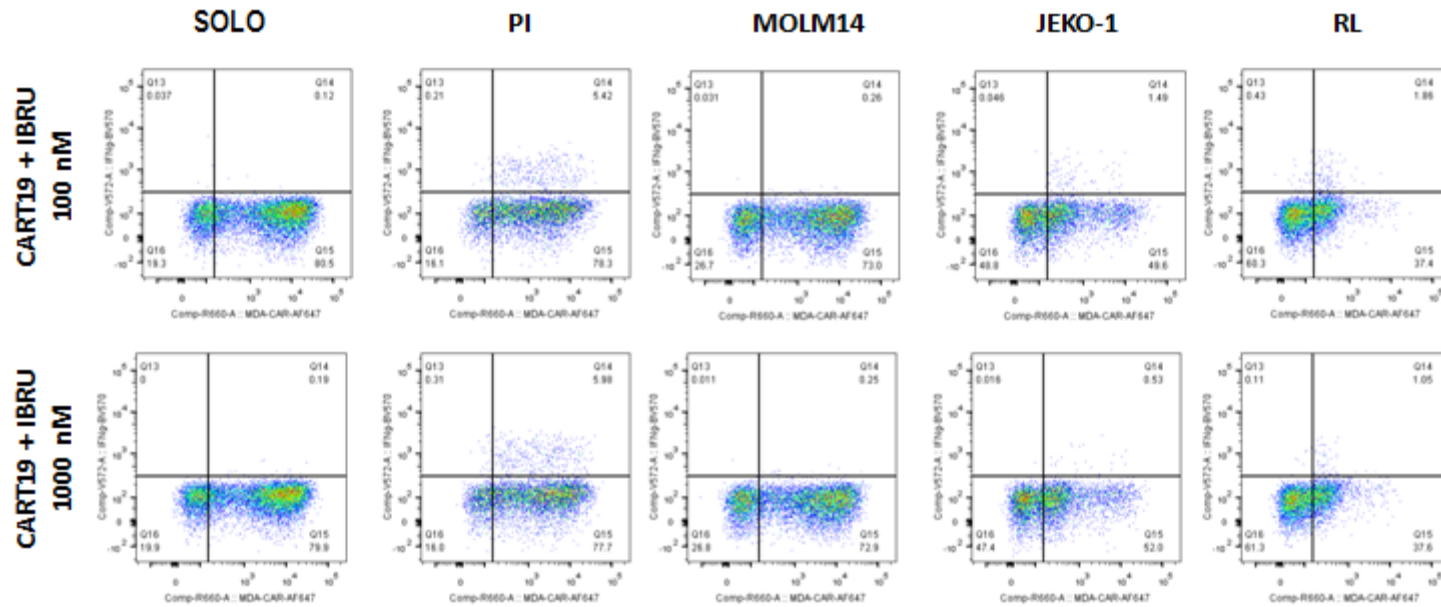
FIG. 14 CONT. **PRODUCCIÓN INTRA-CITOPLASMÁTICA DE IFN $\gamma$** 

FIG. 15

## Secreción de citoquina 72 HR (30-plez LUMINEX)

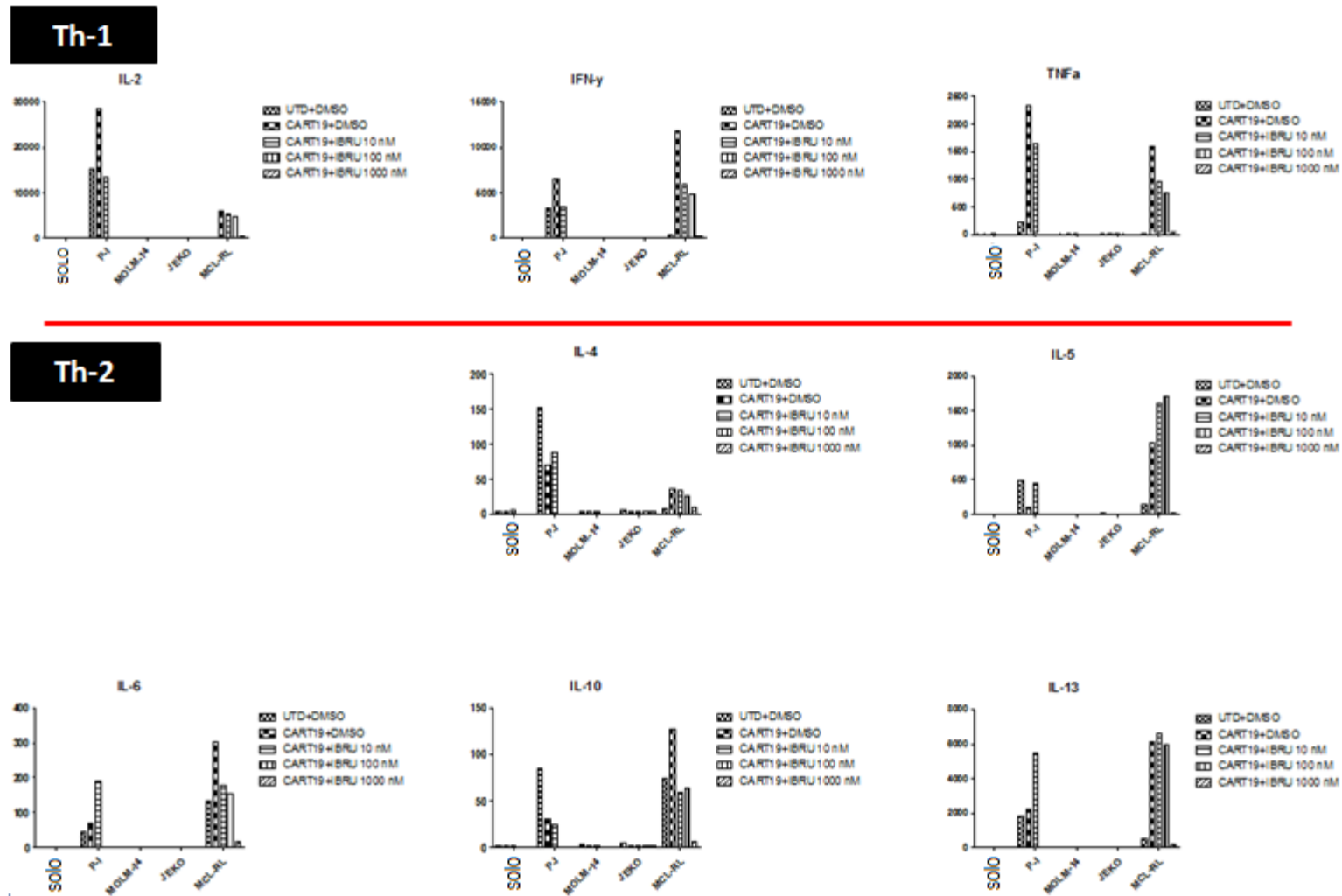


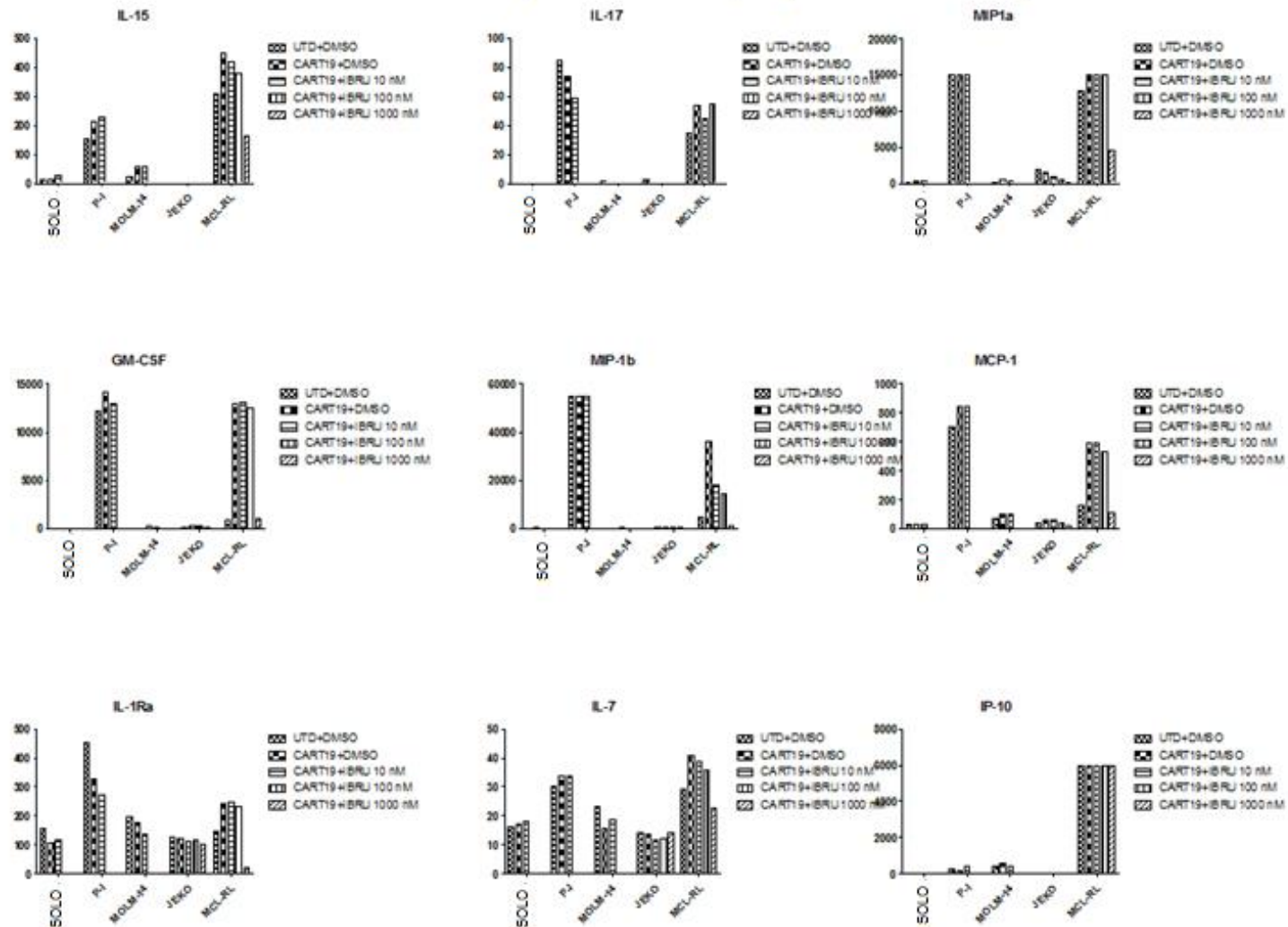
FIG. 15 CONT. **Secreción de citoquina 72 HR (30-plez LUMINEX)**

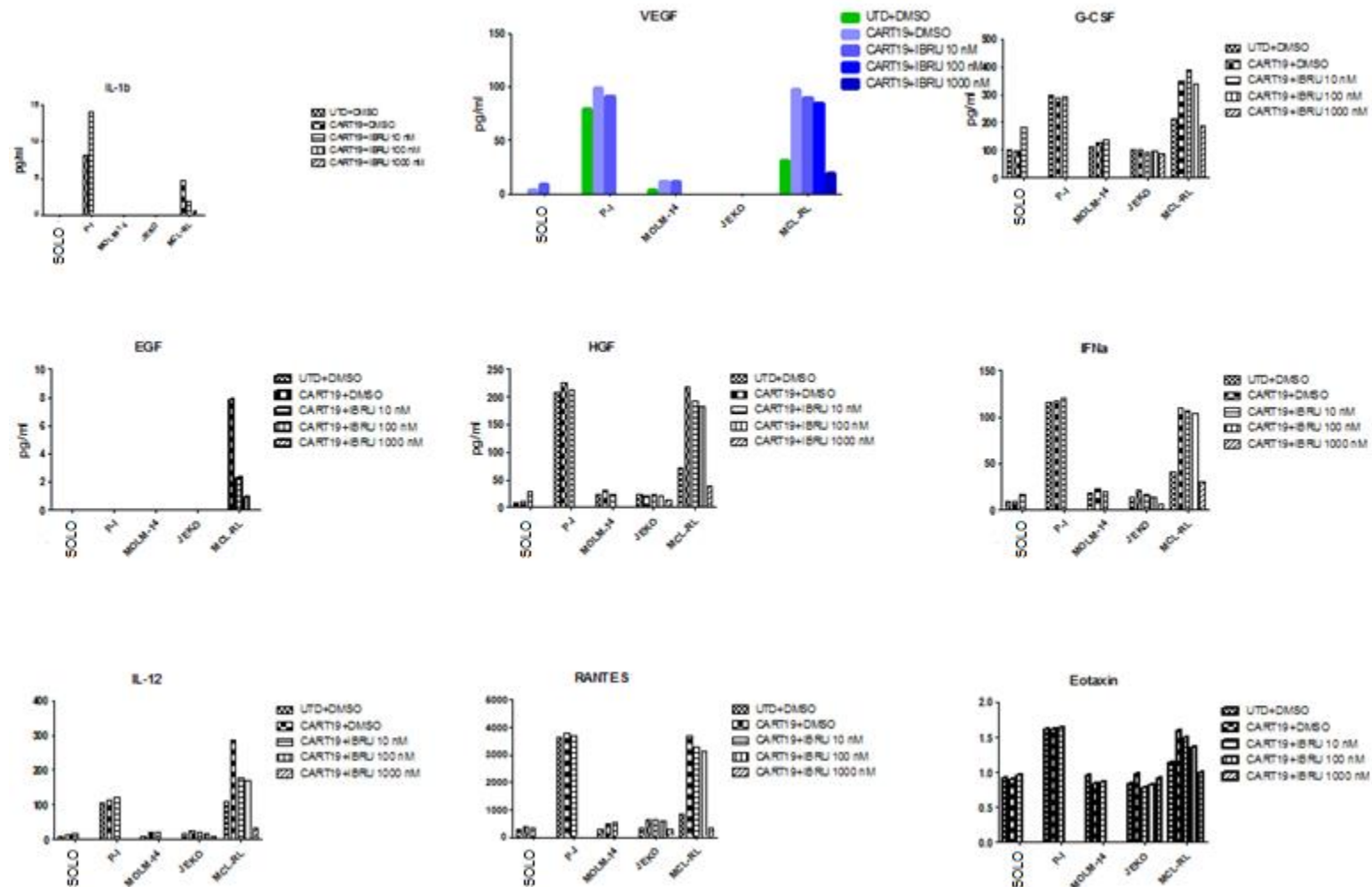
FIG. 15 CONT. **Secreción de citoquina 72 HR (30-plez LUMINEX)**

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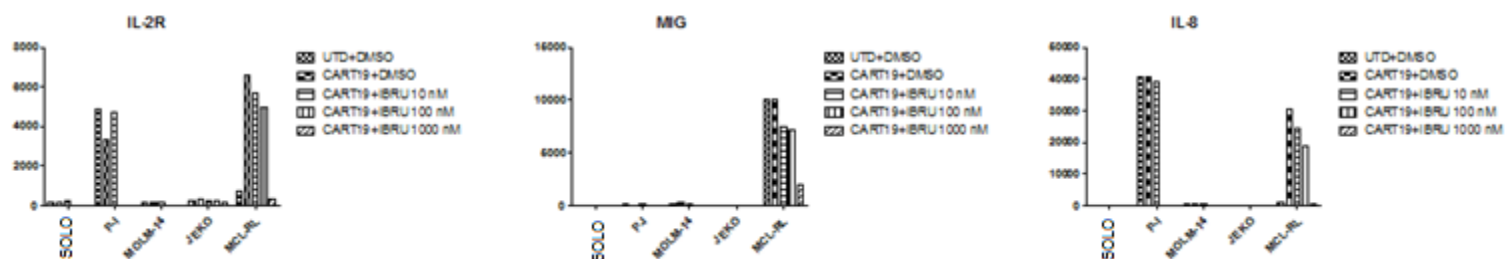


FIG. 16A

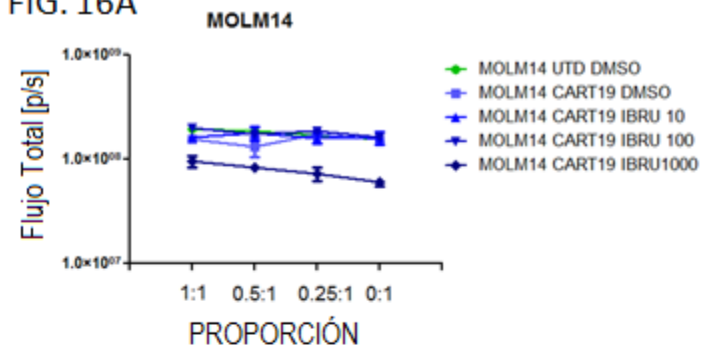


FIG. 16D

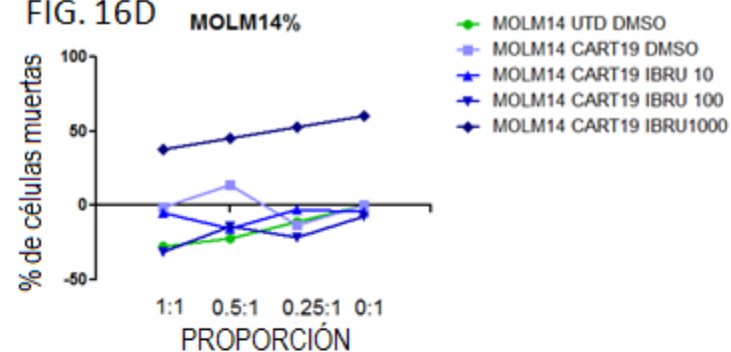


FIG. 16B

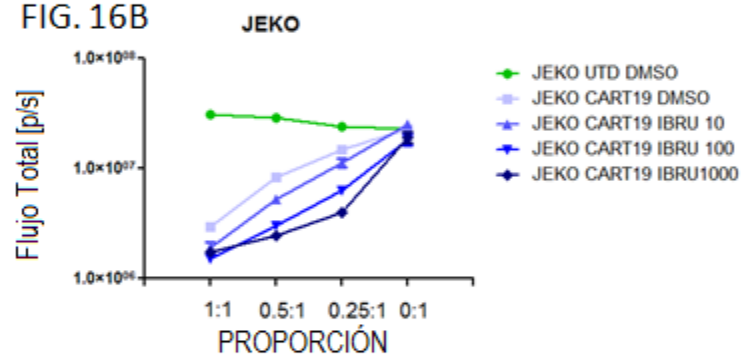


FIG. 16E

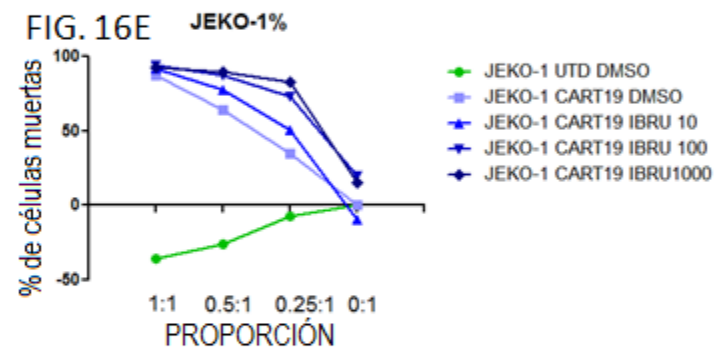


FIG. 16C

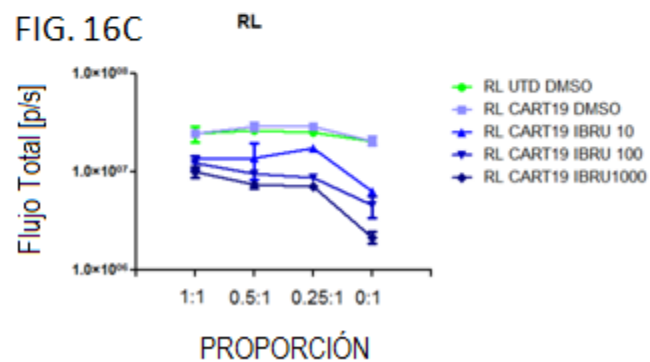
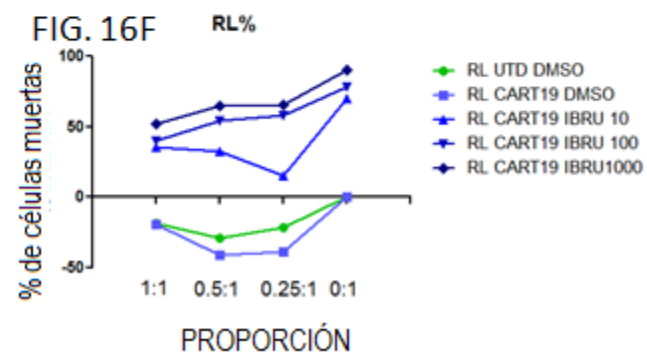


FIG. 16F



## MUERTE EN 24 HORAS MEDIANTE FLUJO

FIG. 17A

MOLM14

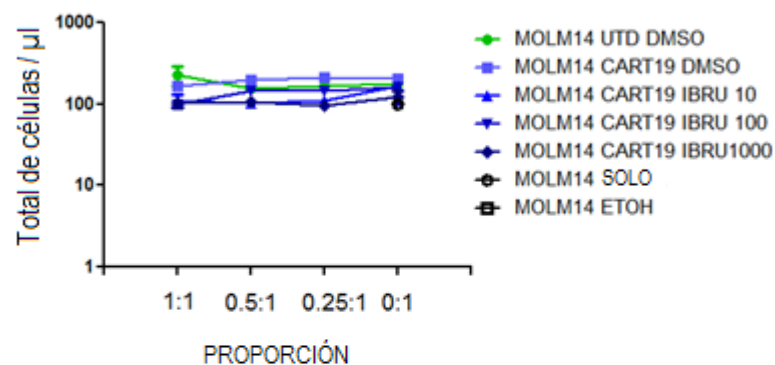


FIG. 17B

JEKO

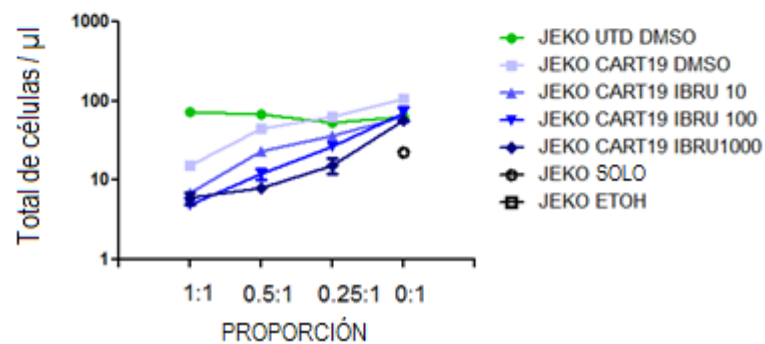
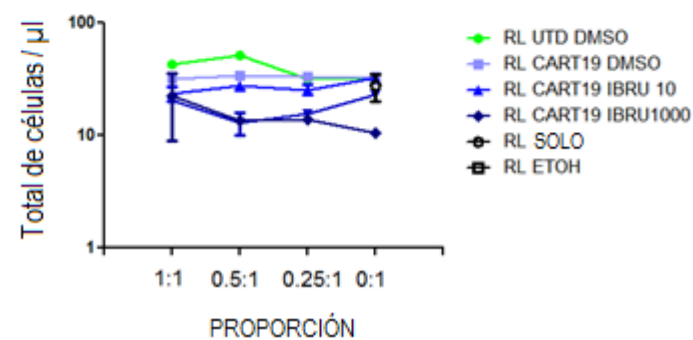


FIG. 17C

RL



## Hallazgo de la dosis de CART19 en el modelo RL MCL: MCL-1

FIG. 18A

MCL-1 BLI

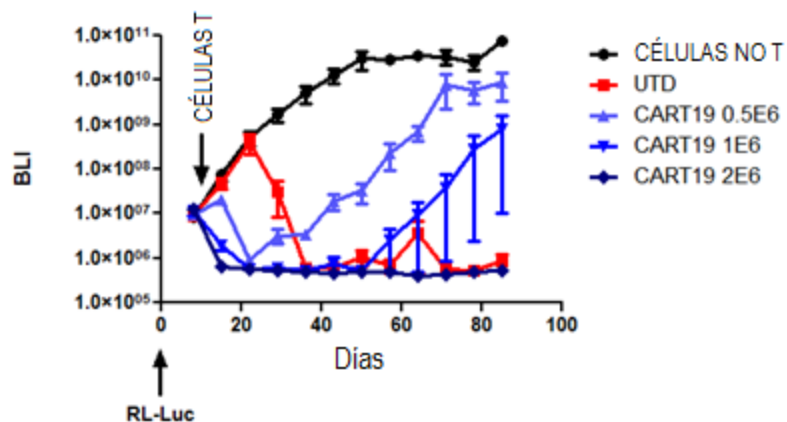


FIG. 18B

MCL-1 BLI

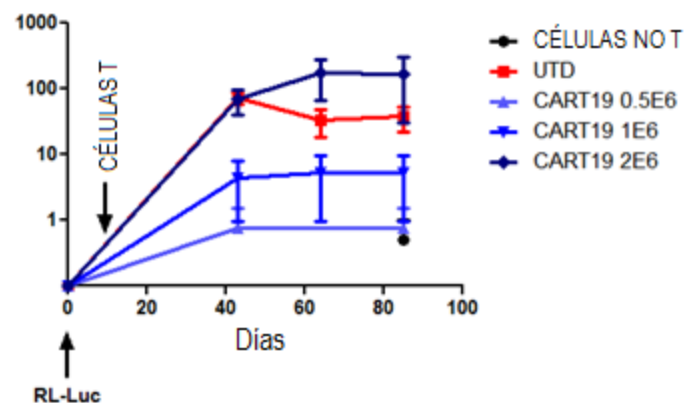


FIG. 18C

MCL-1: OS

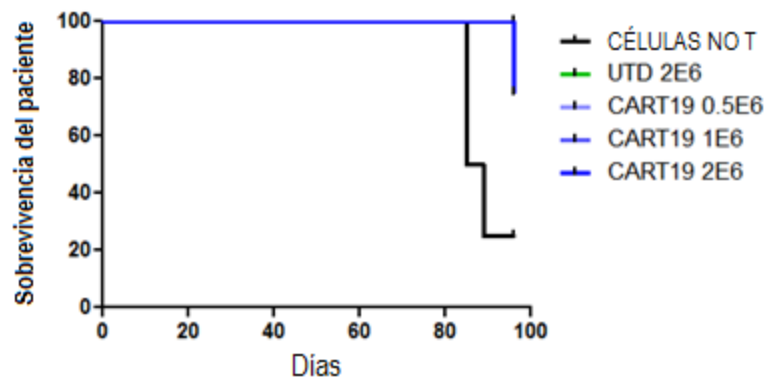
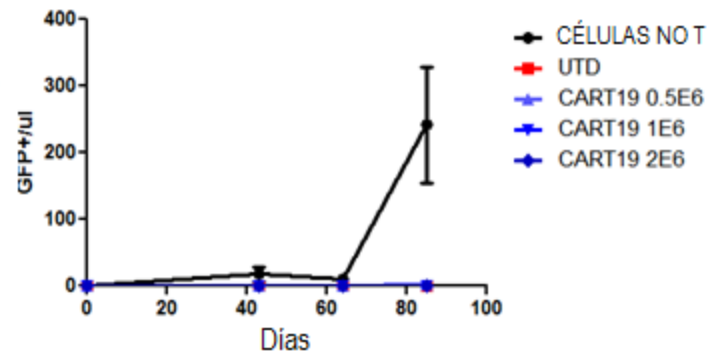


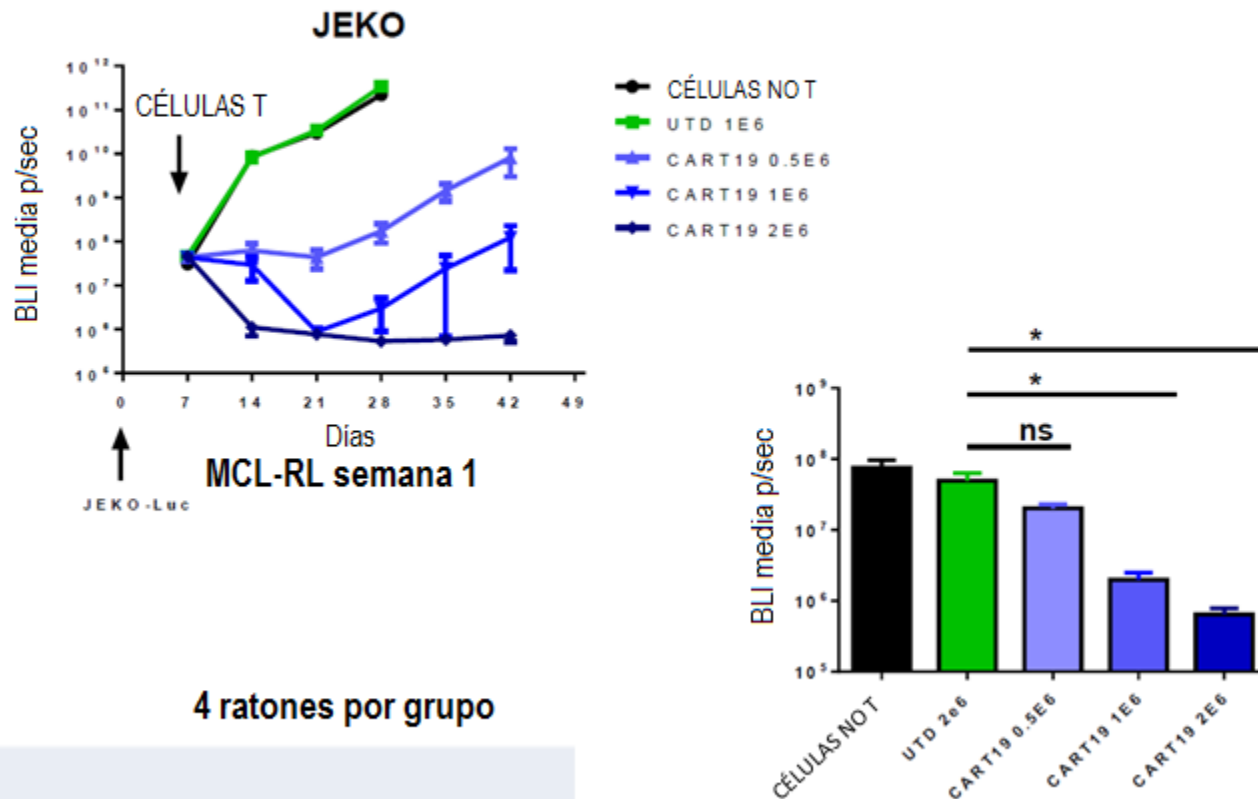
FIG. 18D

RL+ PB



## Hallazgo de la dosis de CART19 en el modelo JEKO-1 MCL: MCL-2

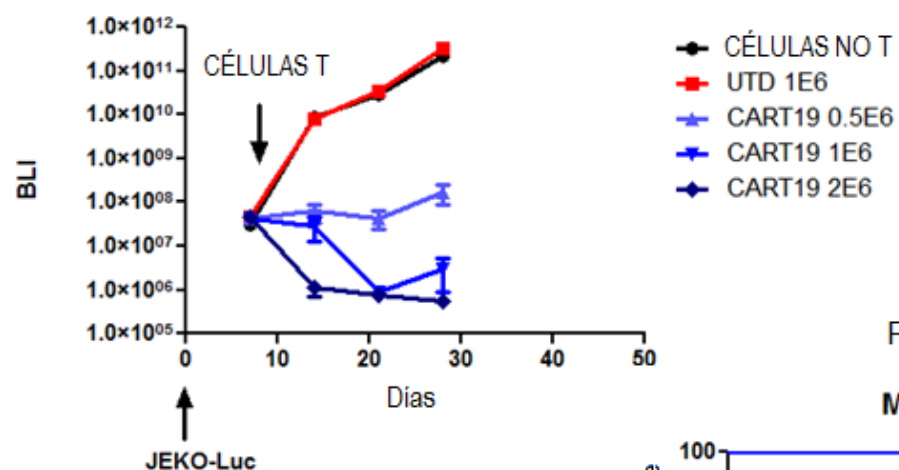
FIG. 19A



JEKO-1-GFP/Células LUC 1e6/día 0 ratón Células T día 7

## Hallazgo de la dosis de CART19 en el modelo JEKO-1 MCL: MCL-2

FIG. 19A



JEKO-1-GFP/Células LUC 1e6/día 0 ratón Células T día 7

FIG. 19B

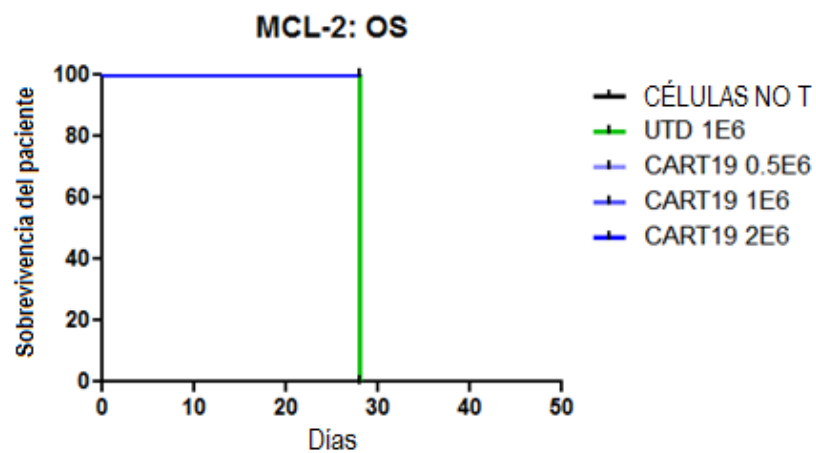
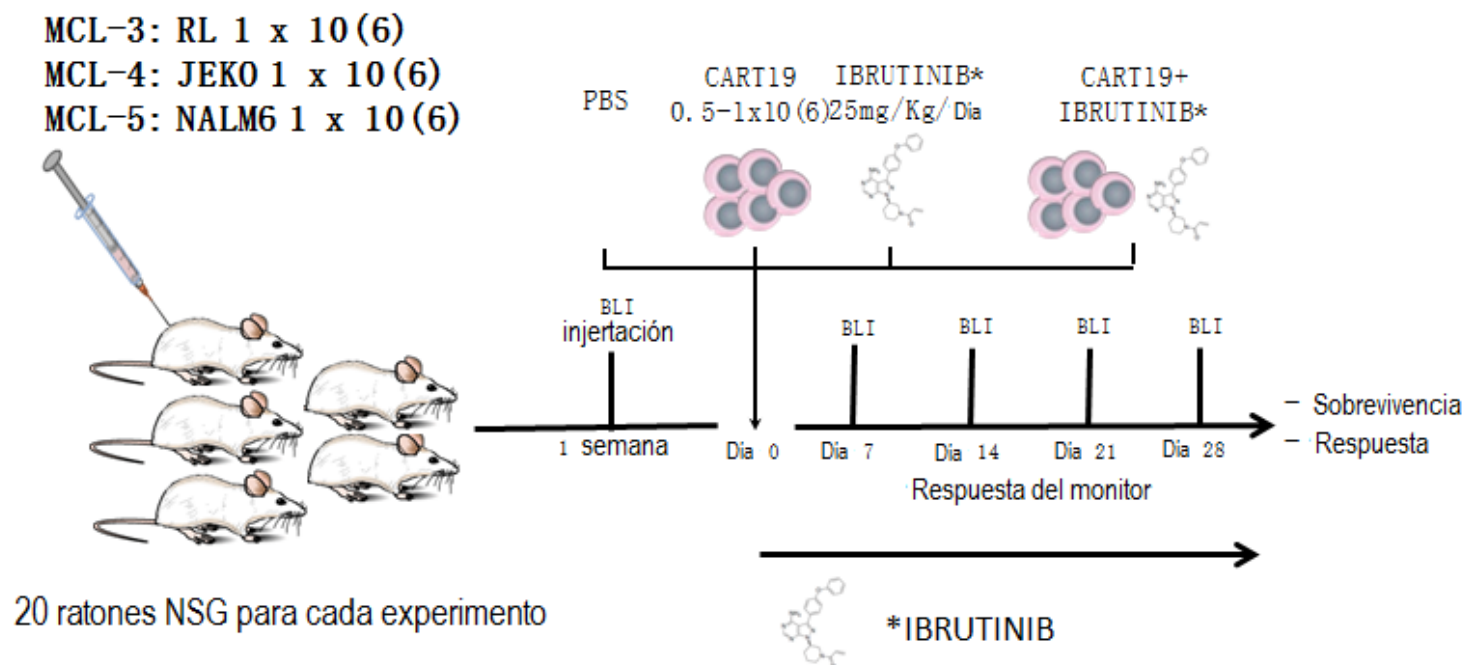
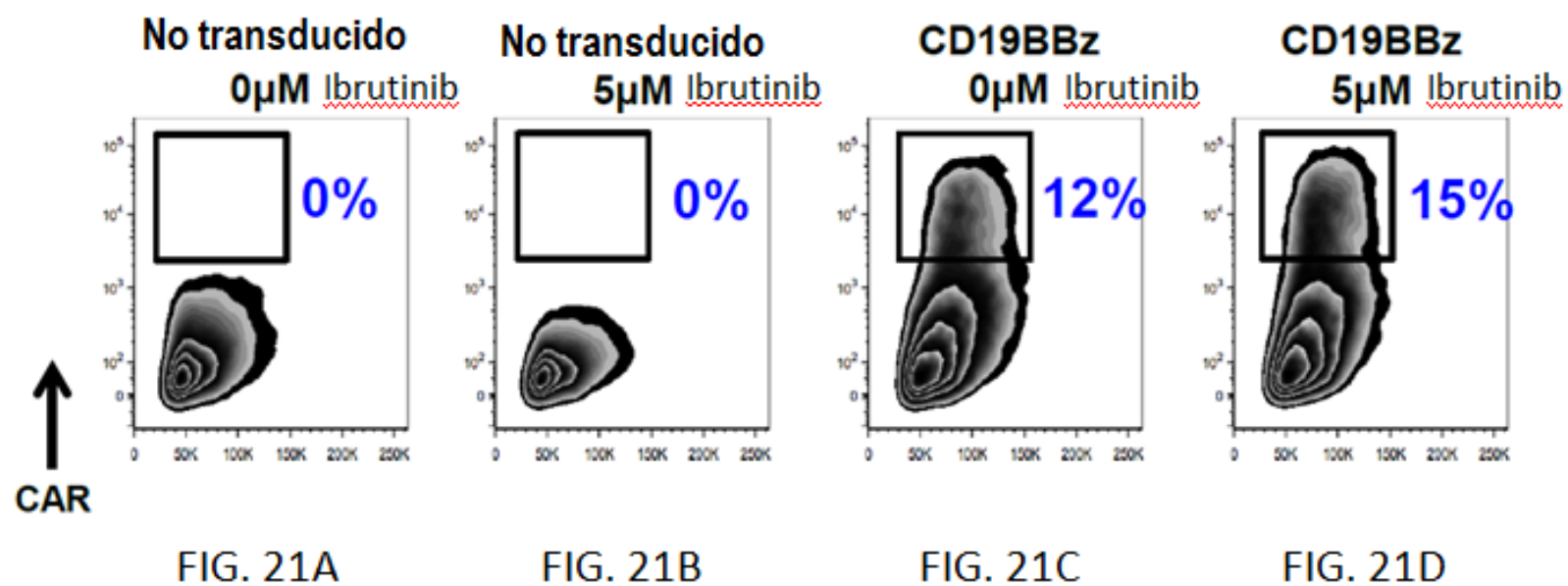


FIG. 20

## Actividad in vivo de CART19 e Ibrutinib: MCL - 3,4,5





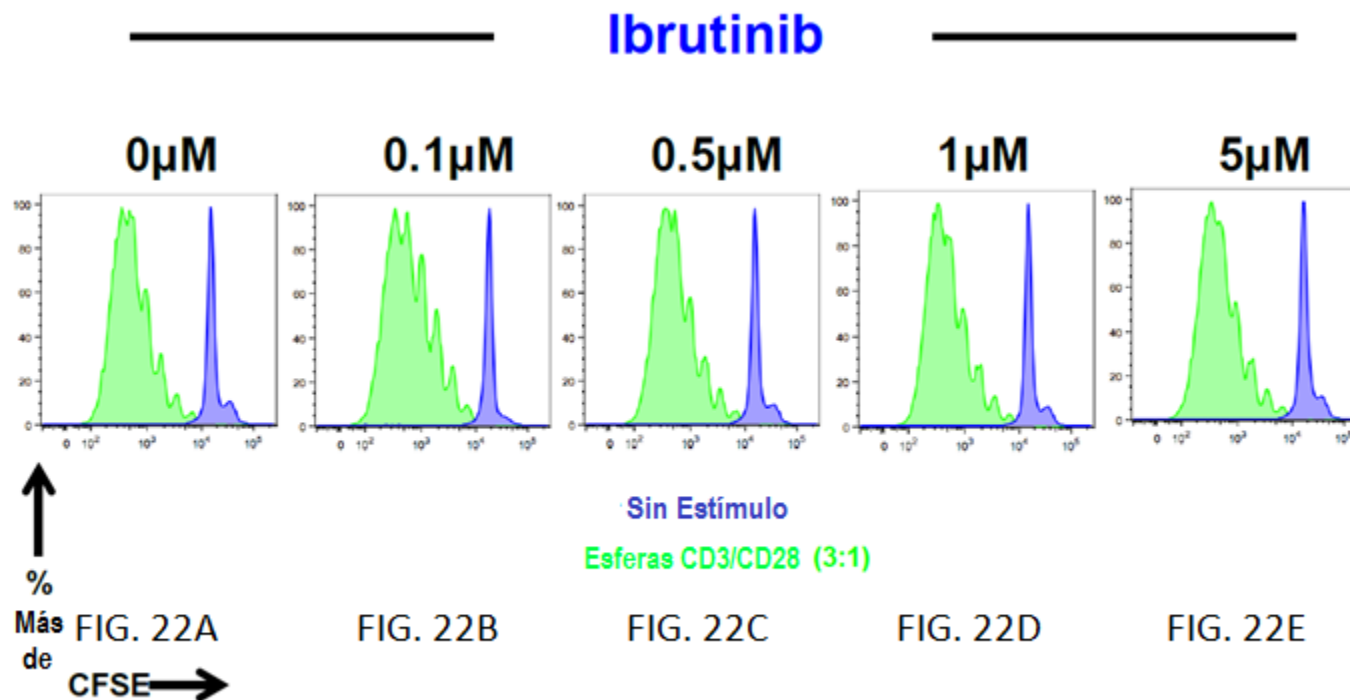


FIG. 23

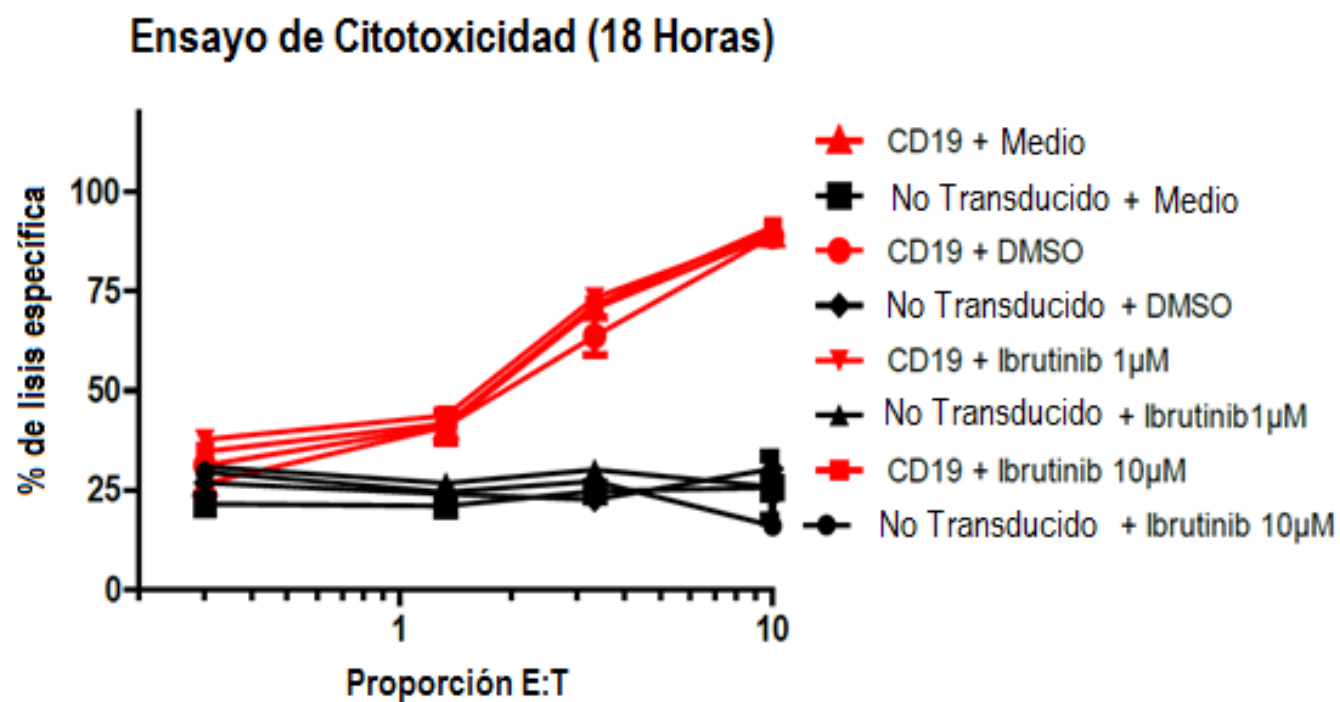


FIG 24.

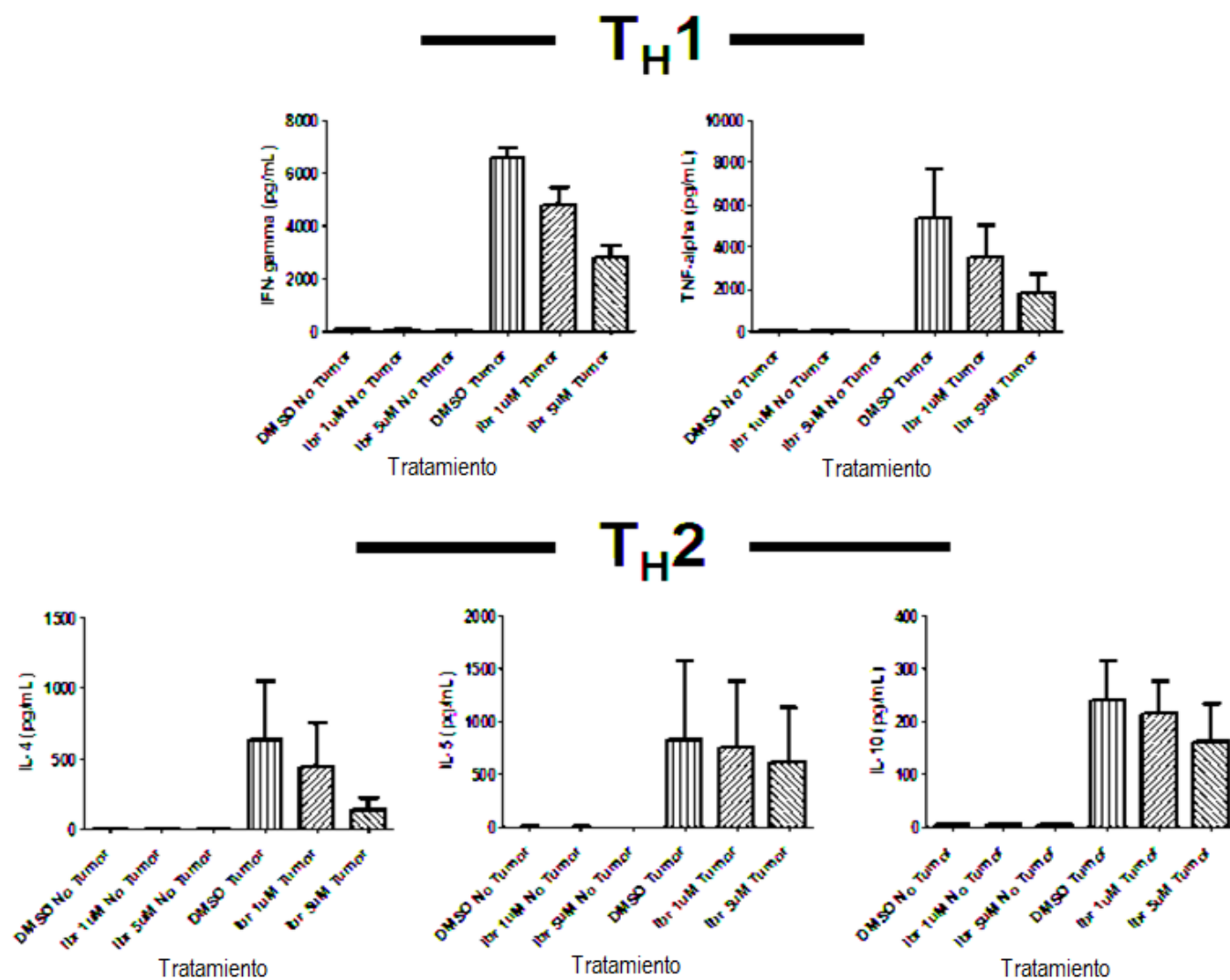


FIG. 25A

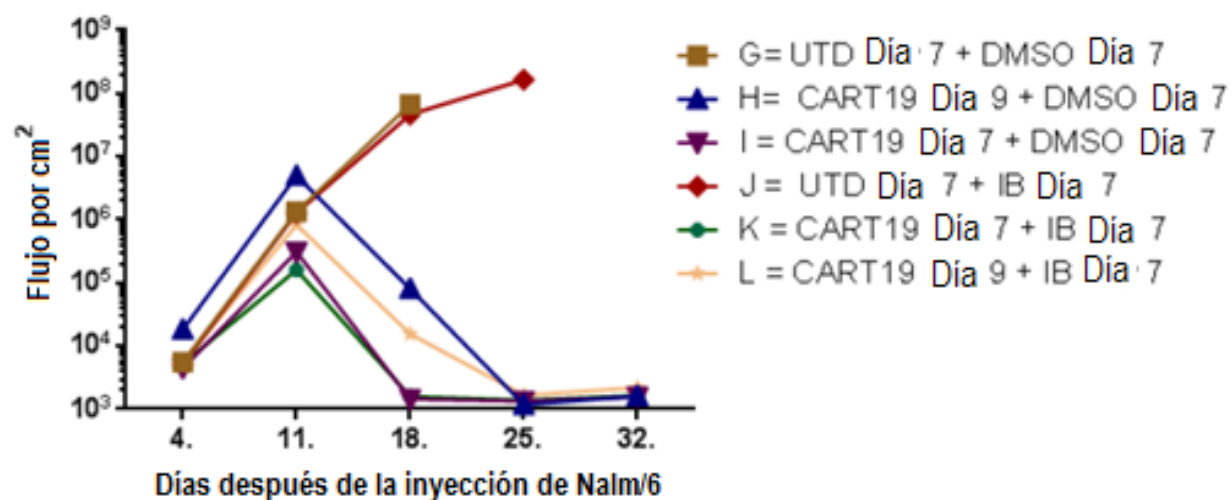
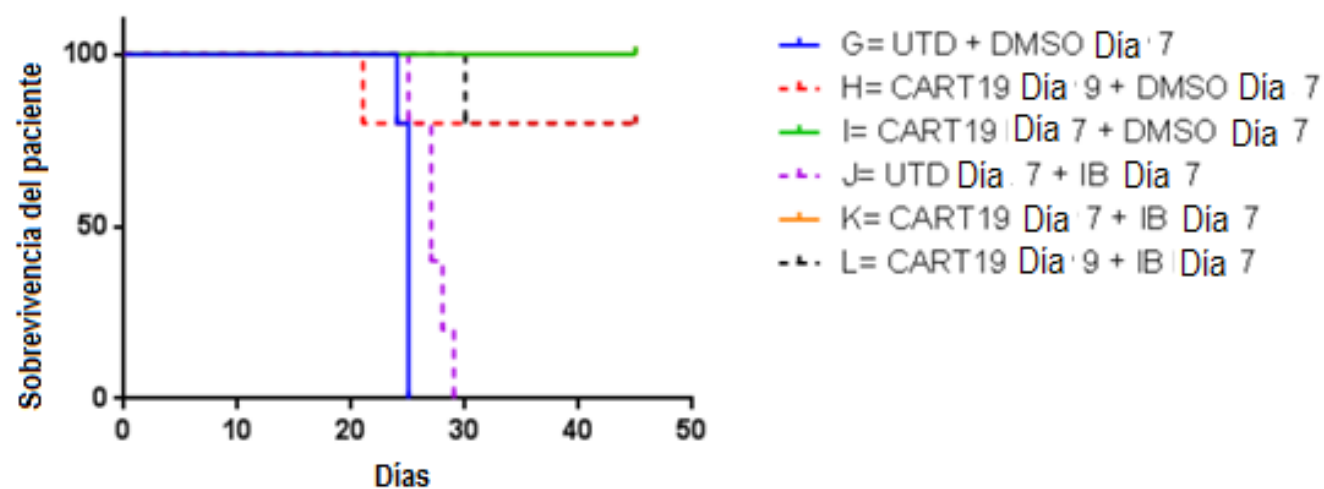


FIG. 25B



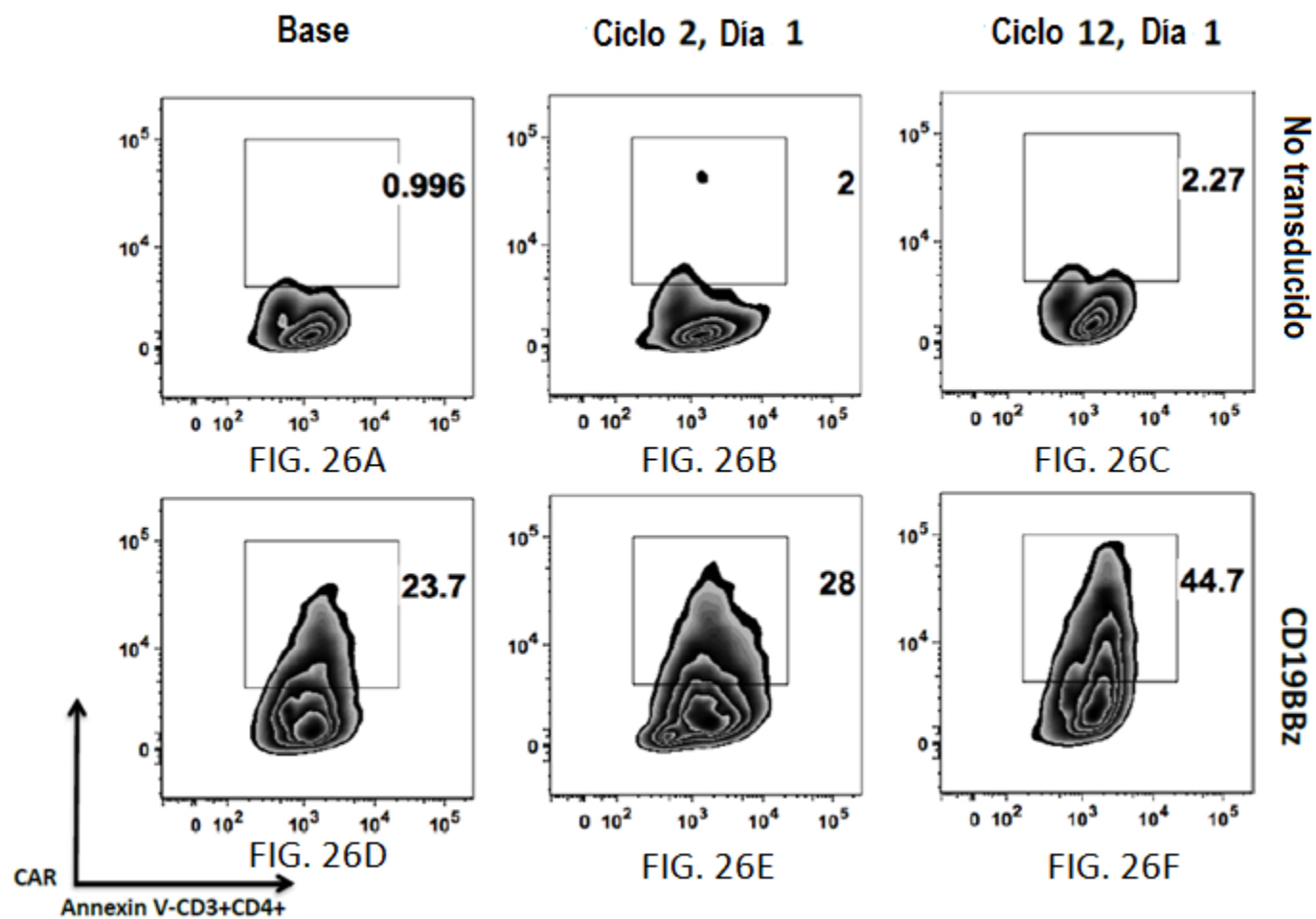
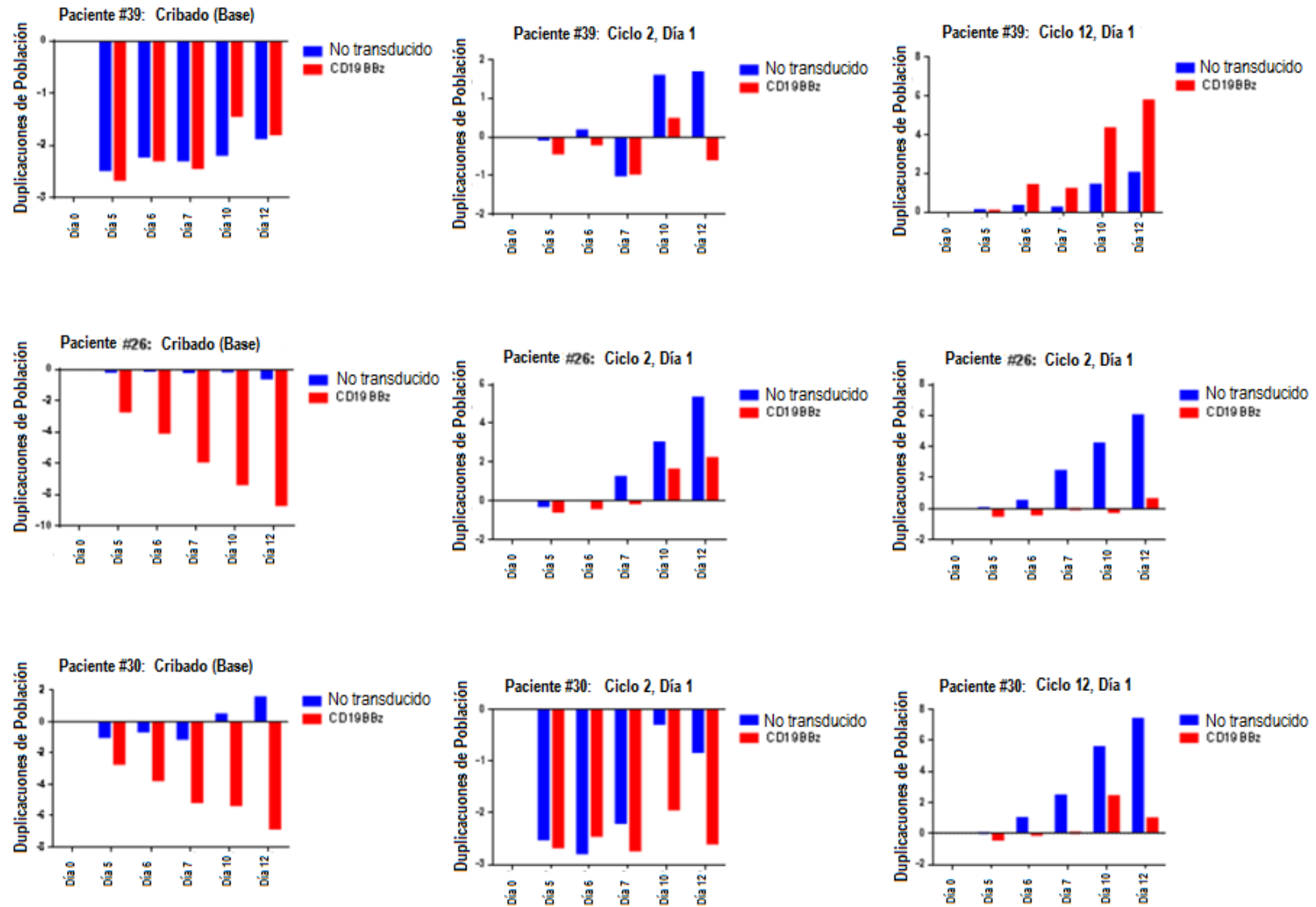
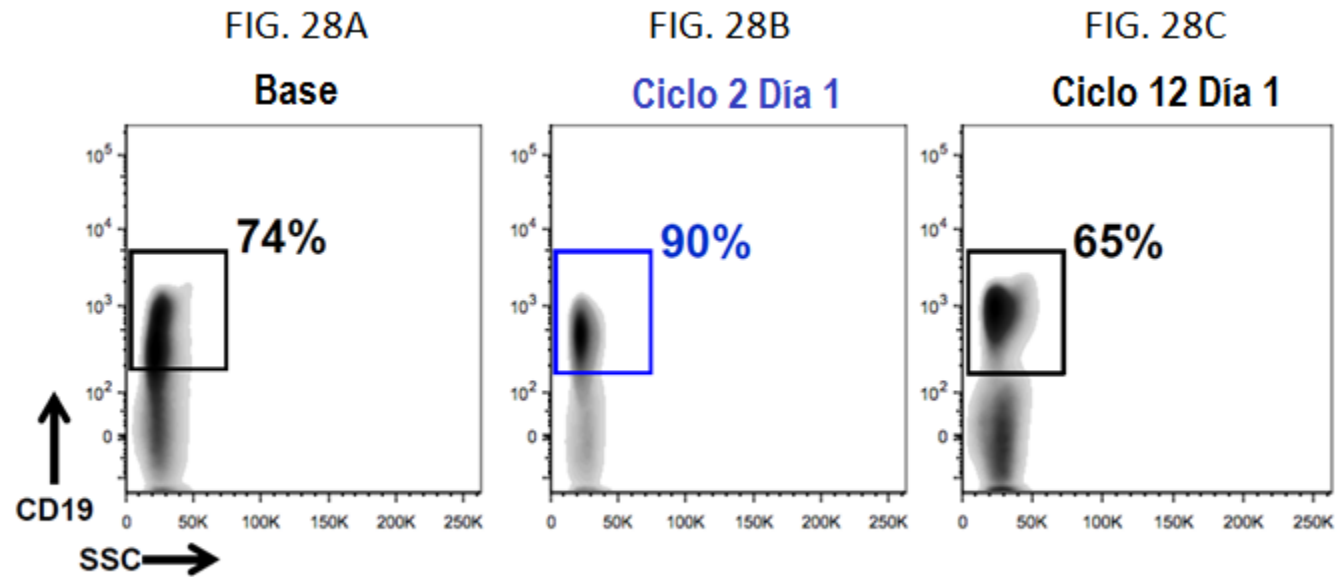


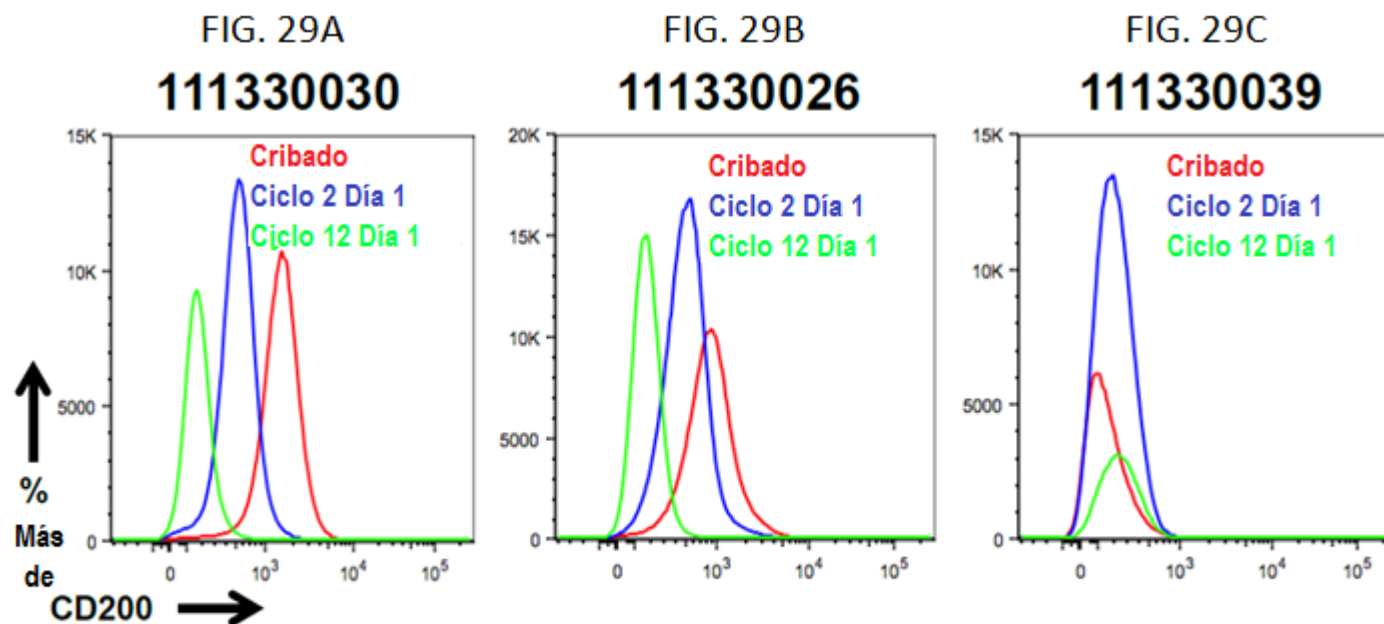


FIG 27





llevado a cabo en singuletes, fsc-ssc, anexina-



llevado a cabo en fsc/scc, anexina-CD19+

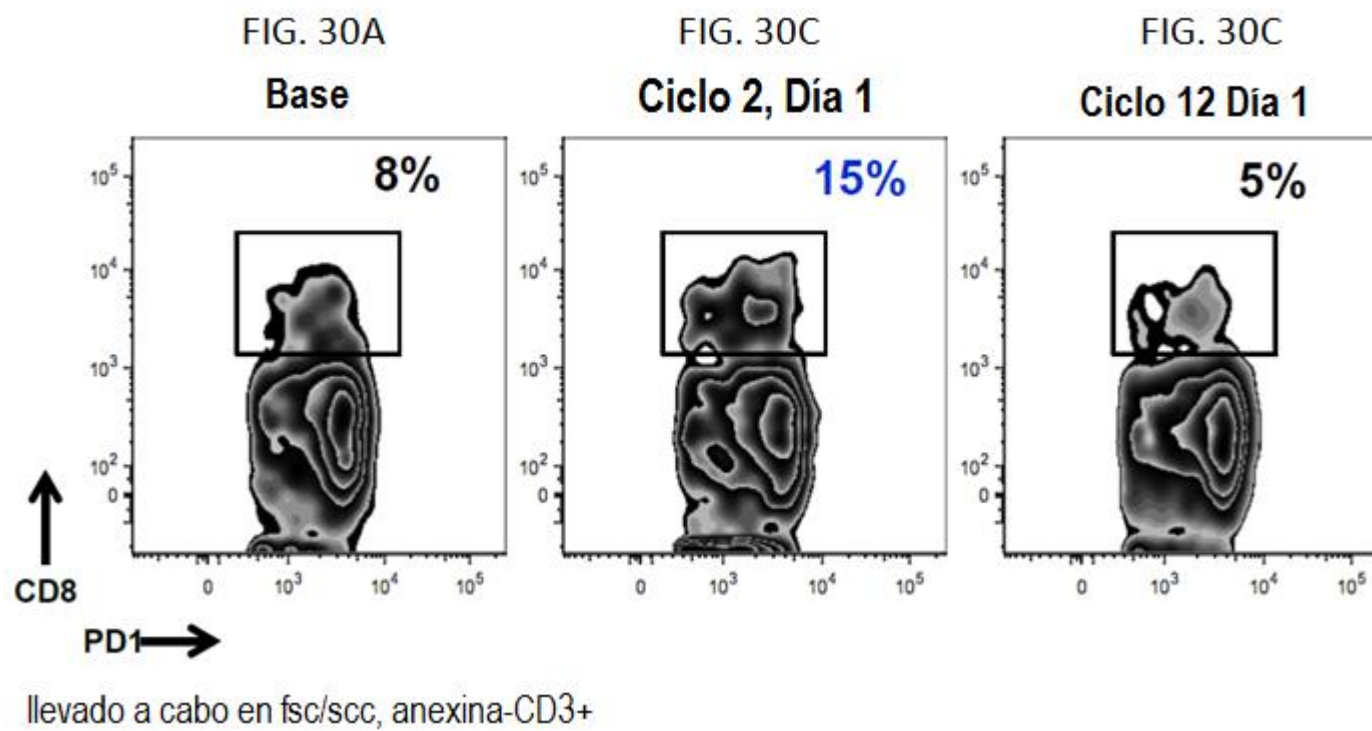
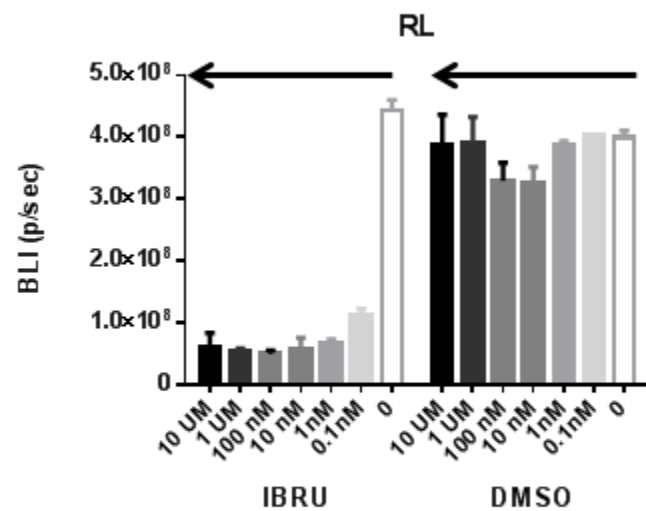
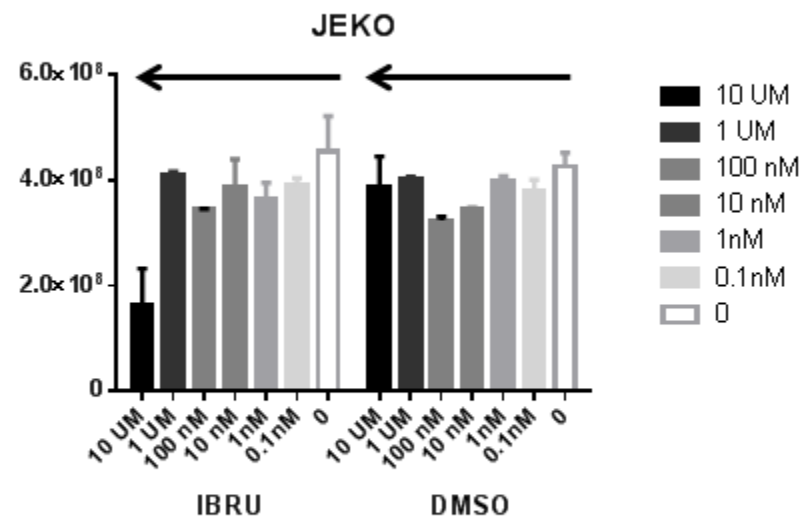


FIG. 31A



Sensible a Ibrutinib

FIG. 31B



Resistente a Ibrutinib

FIG. 32

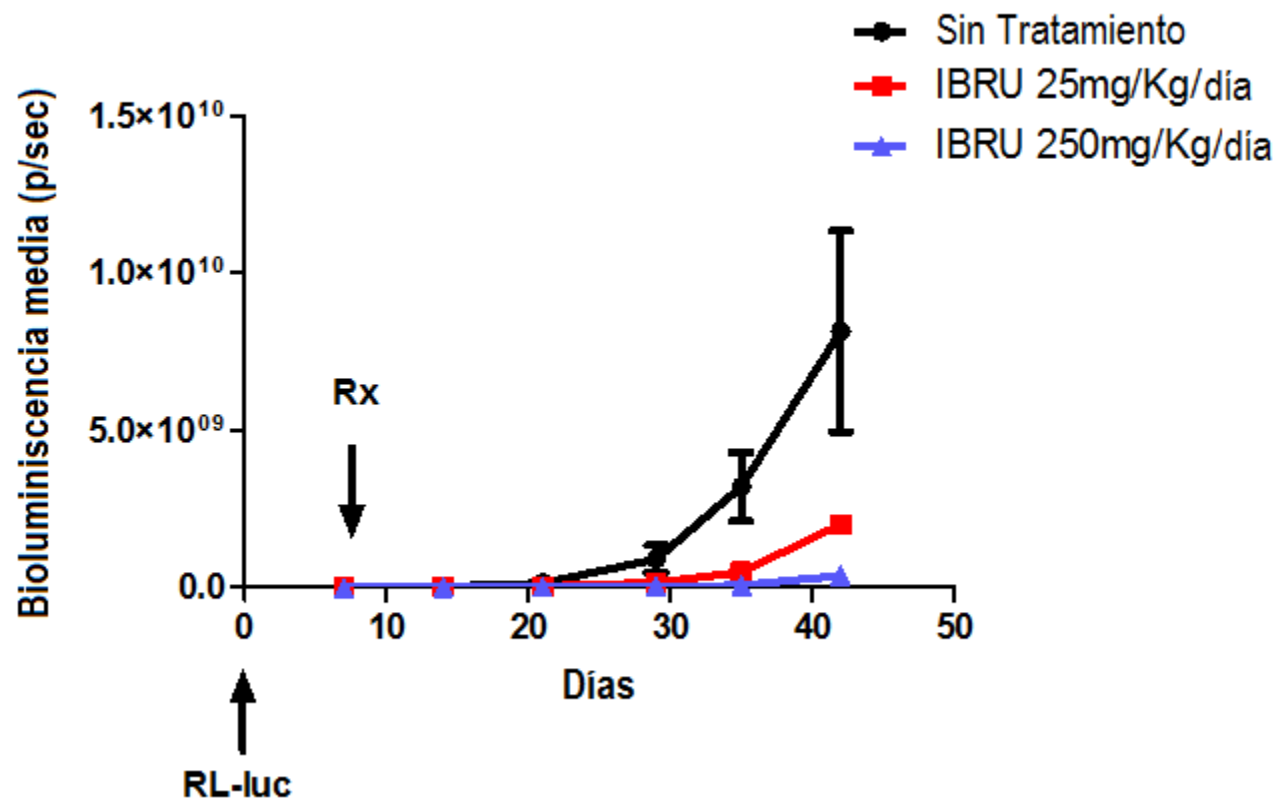


FIG. 33

Tinción de CD19

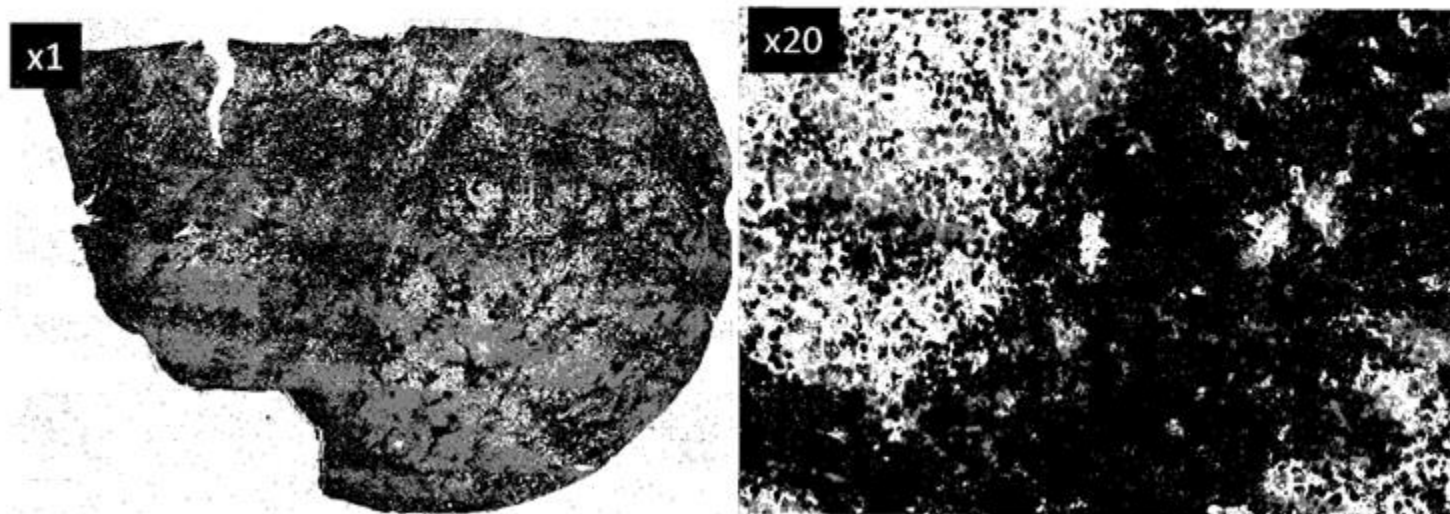


FIG. 34

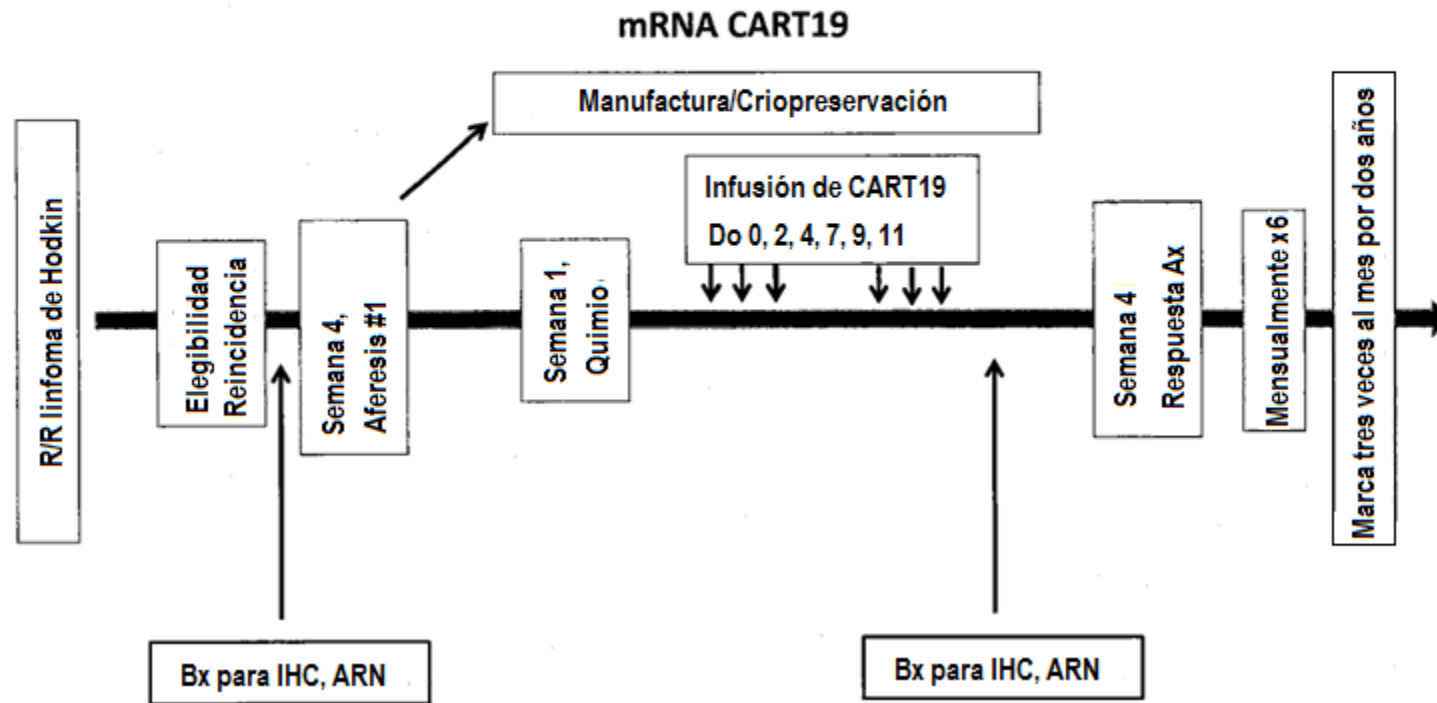


FIG. 35

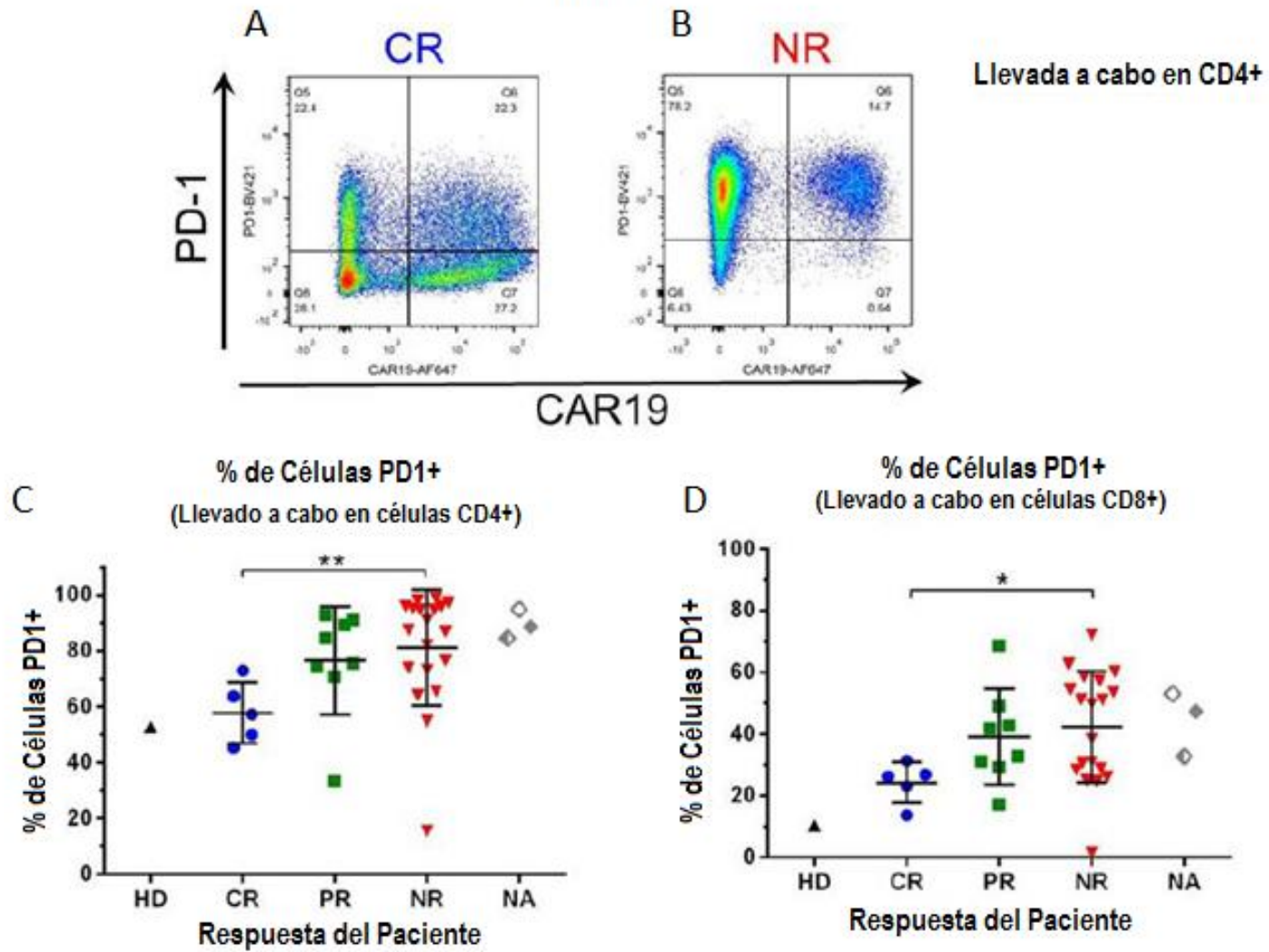


FIG. 36

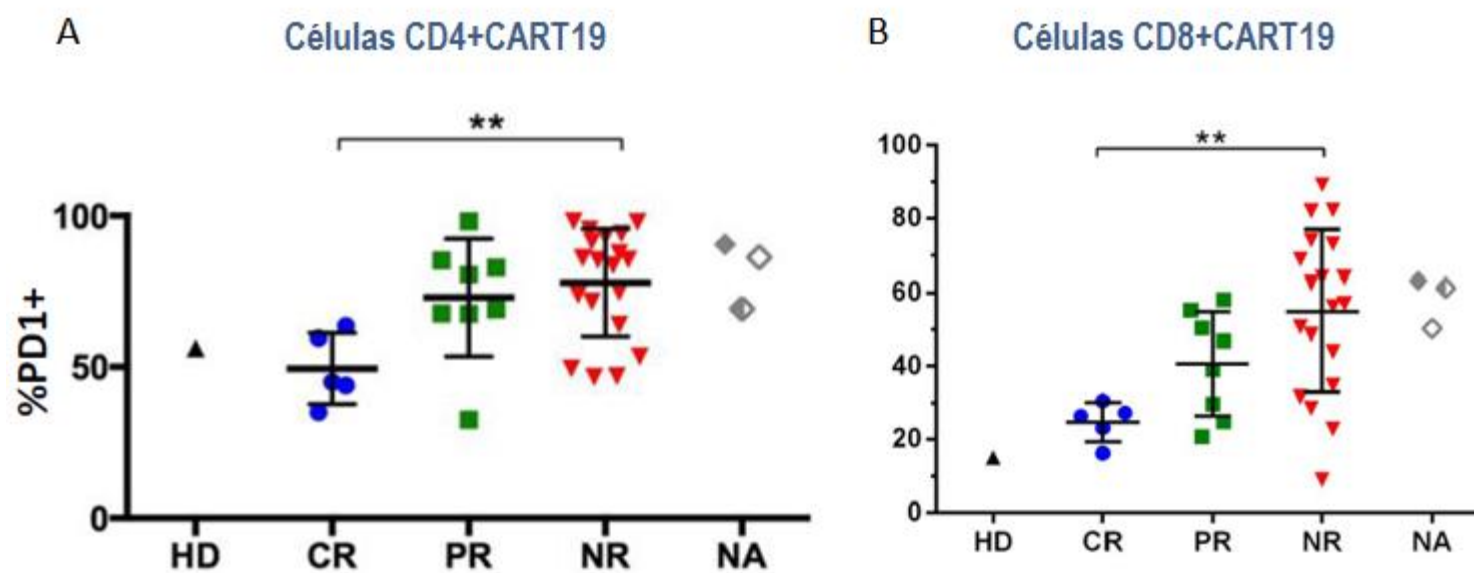


FIG 37.

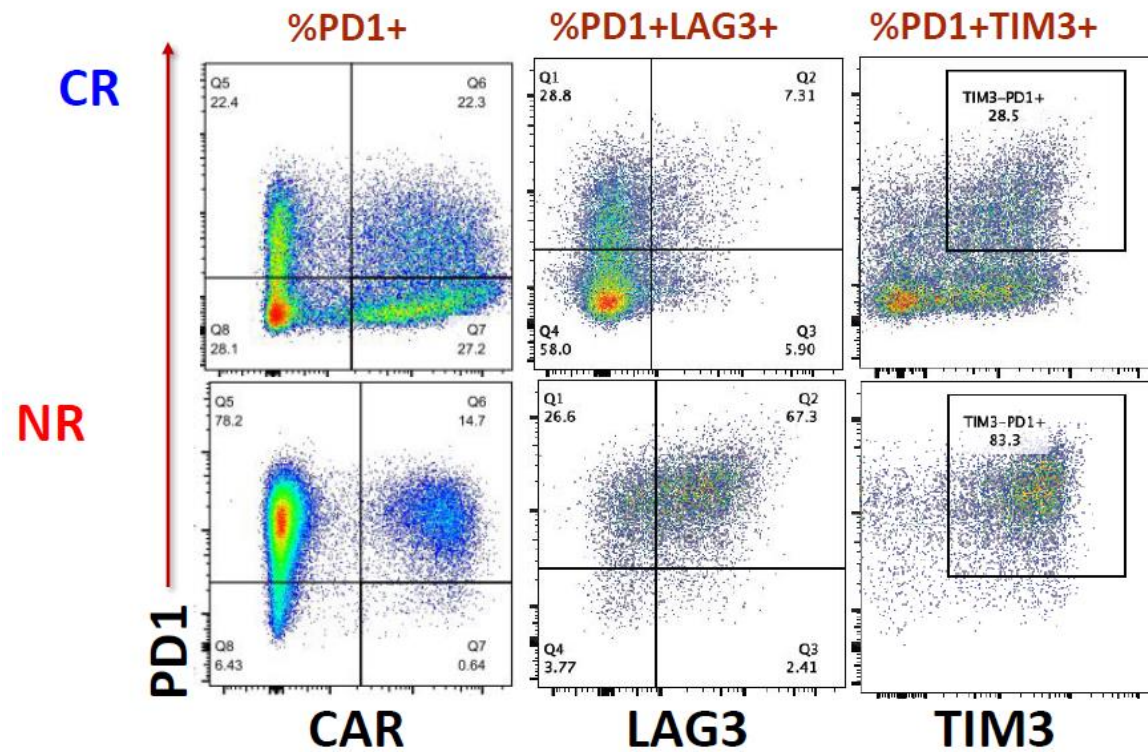


FIG. 38

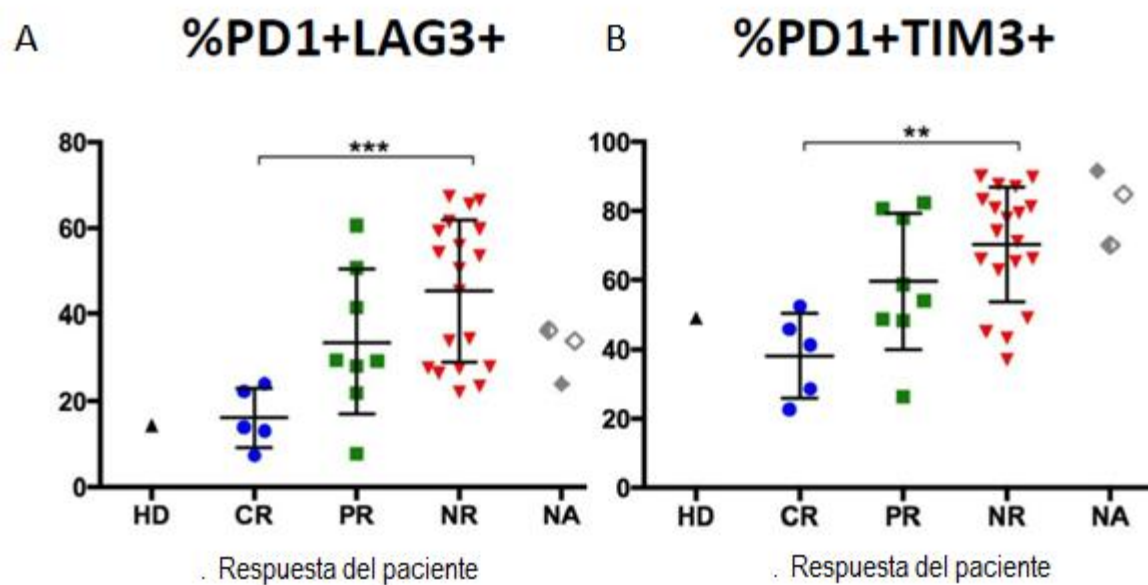


FIG. 39

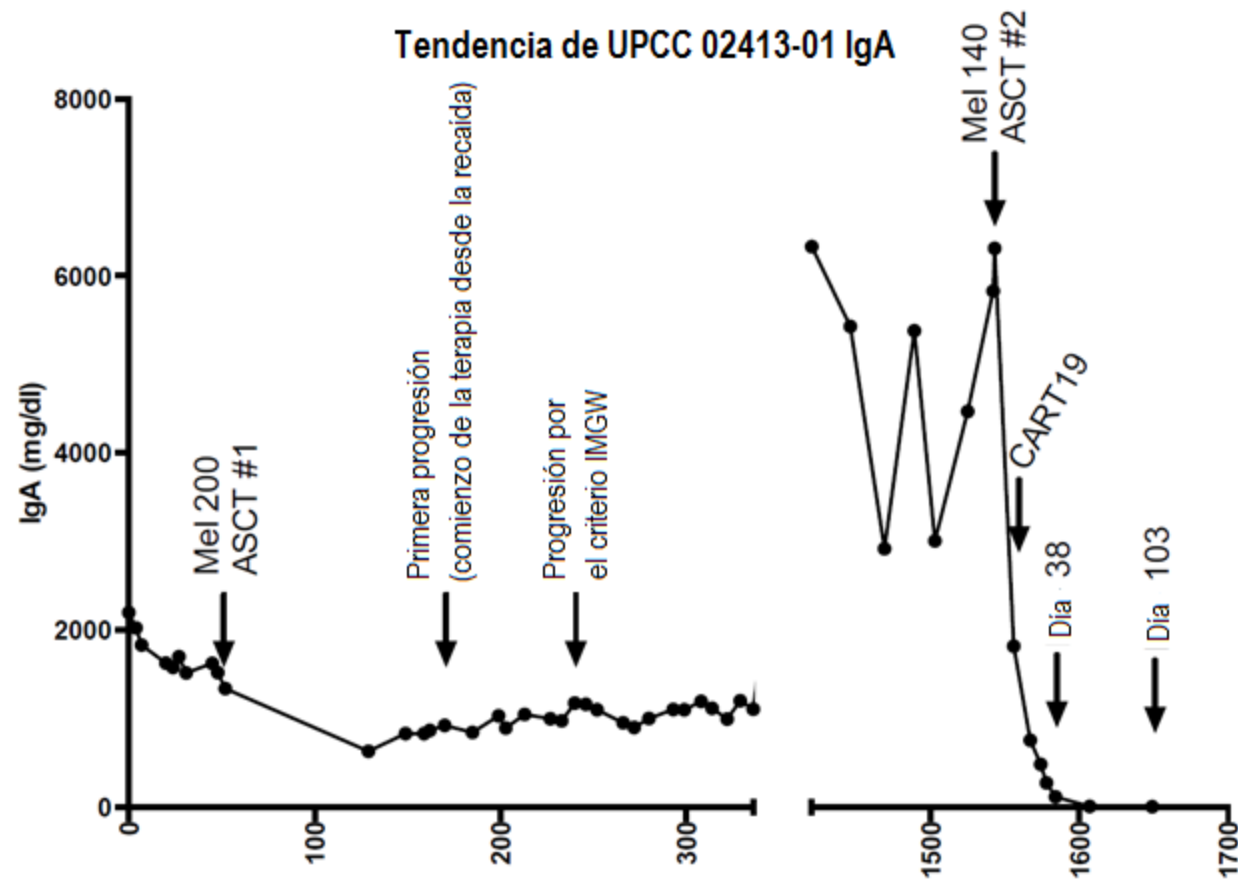


FIG. 40

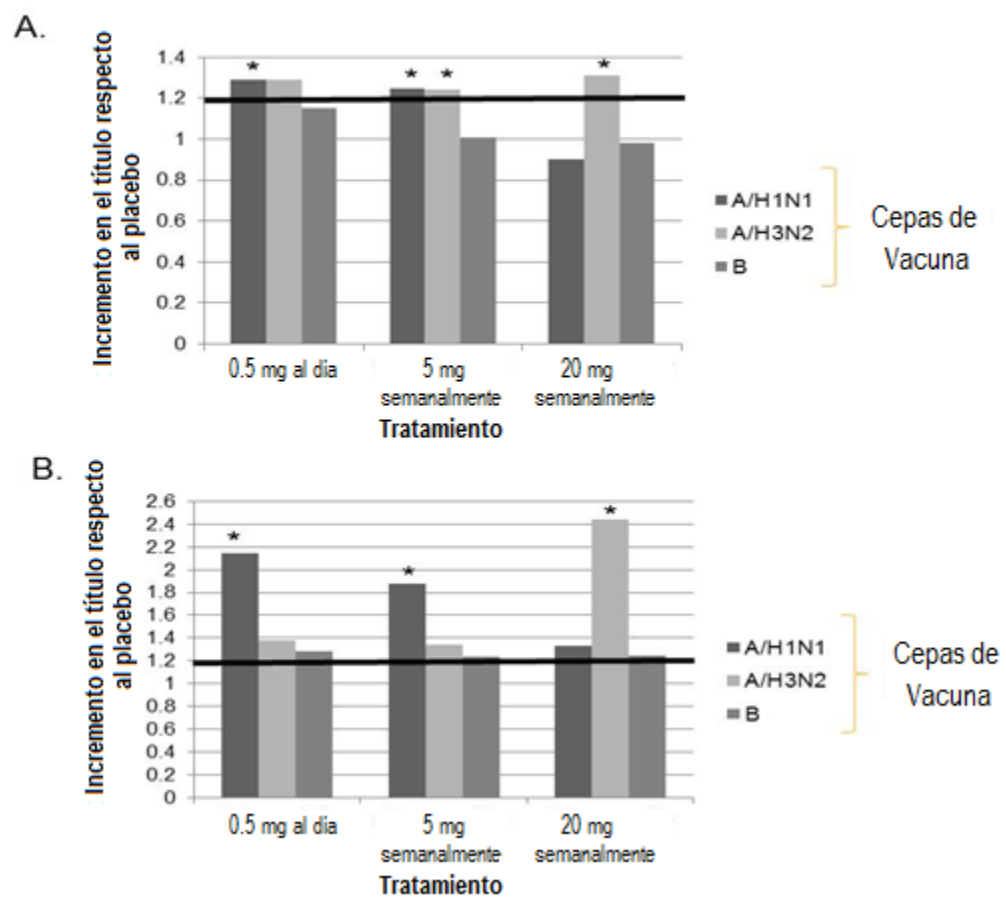


FIG. 41

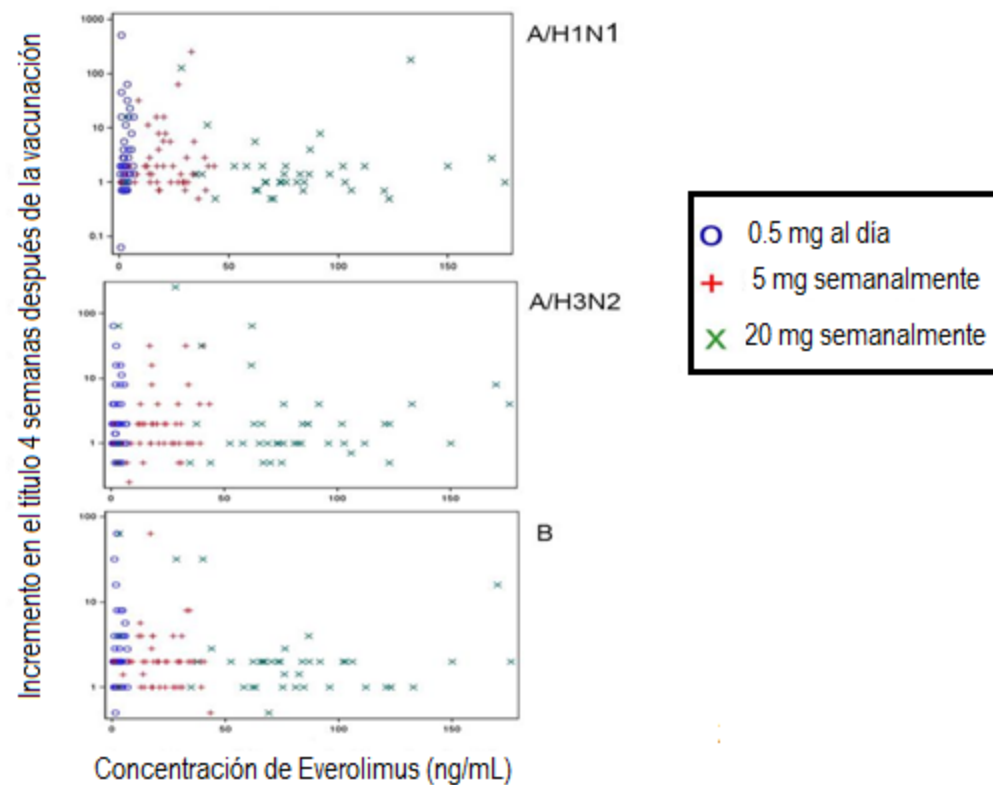


FIG. 42

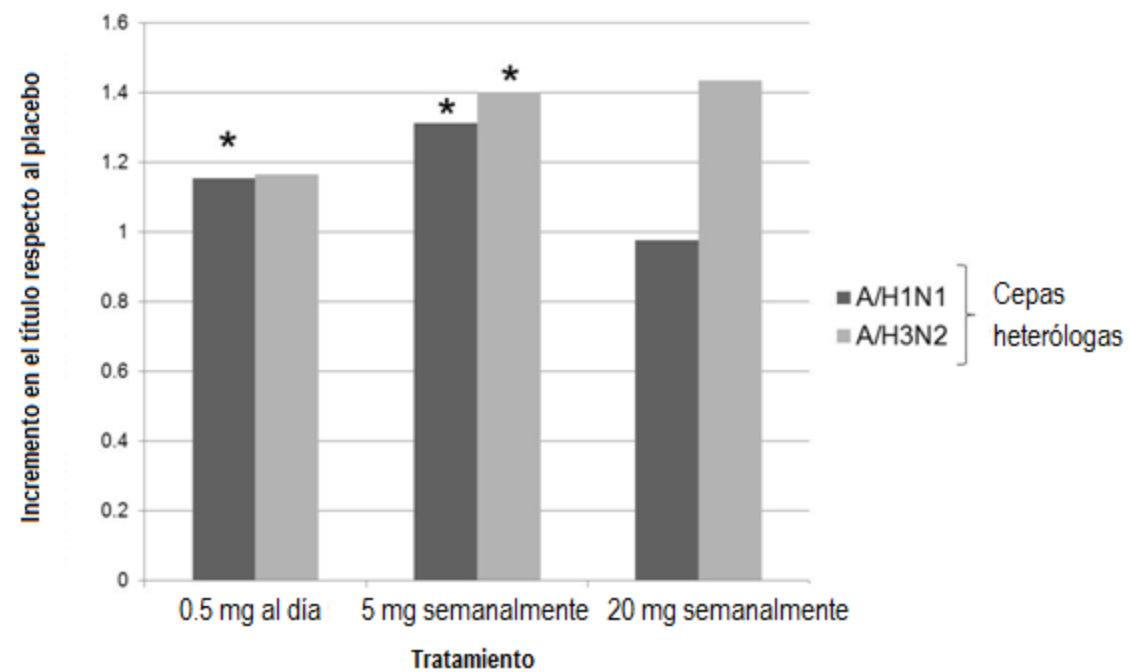
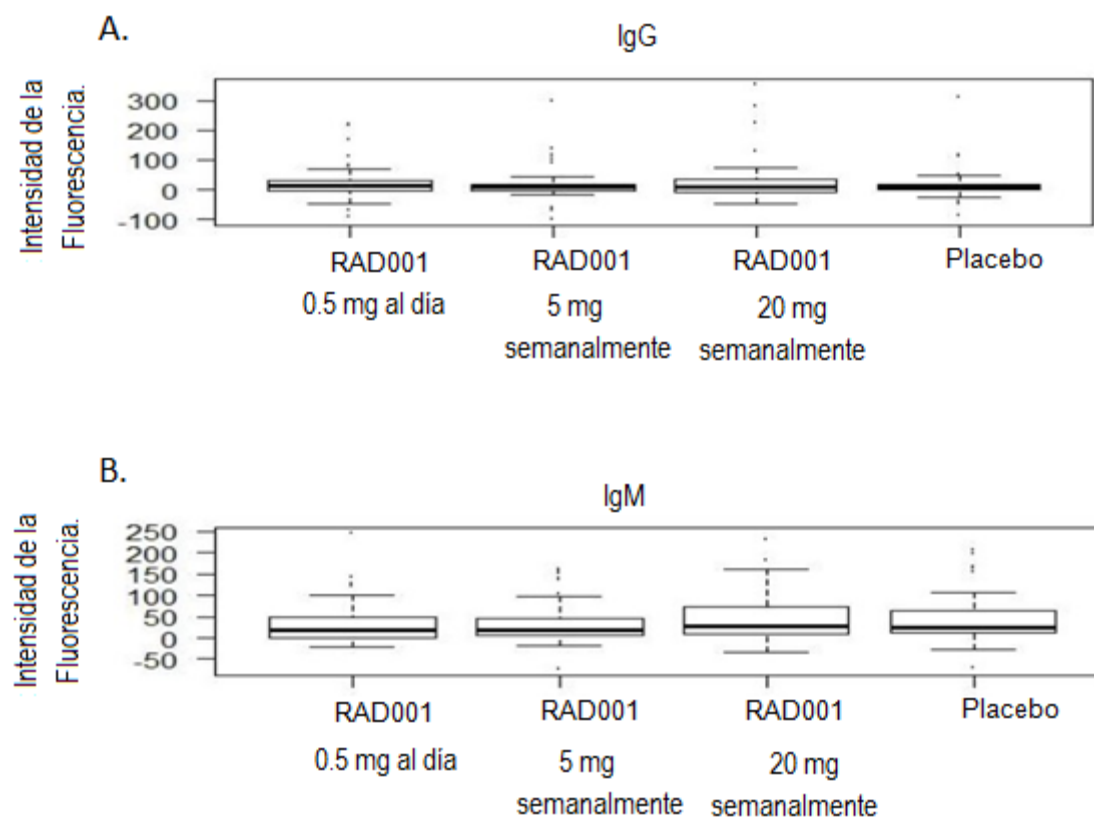


FIG. 43





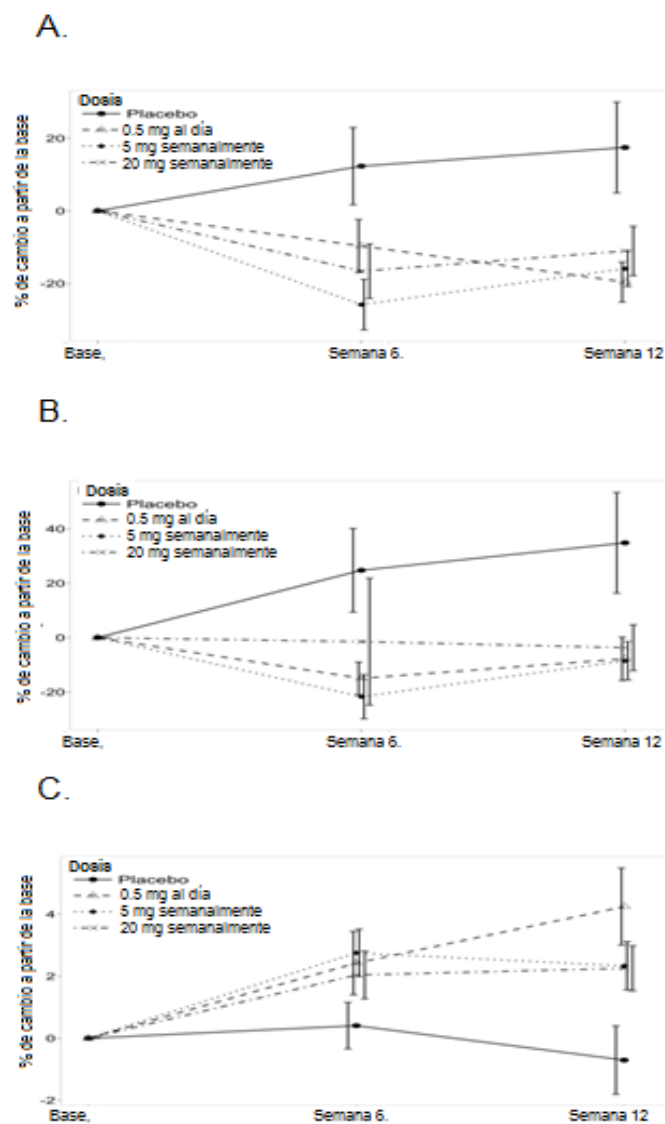
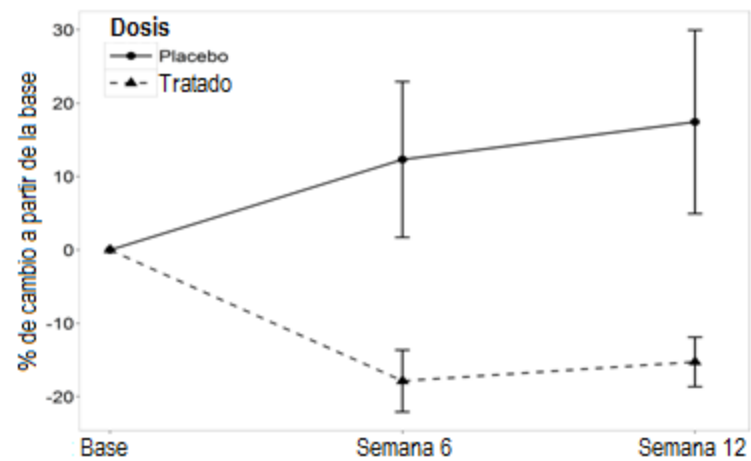


FIG 44

FIG. 45

A.



B.

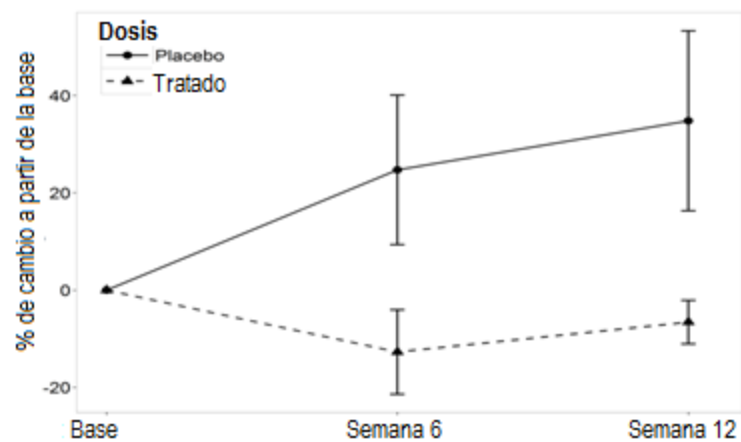


FIG. 46

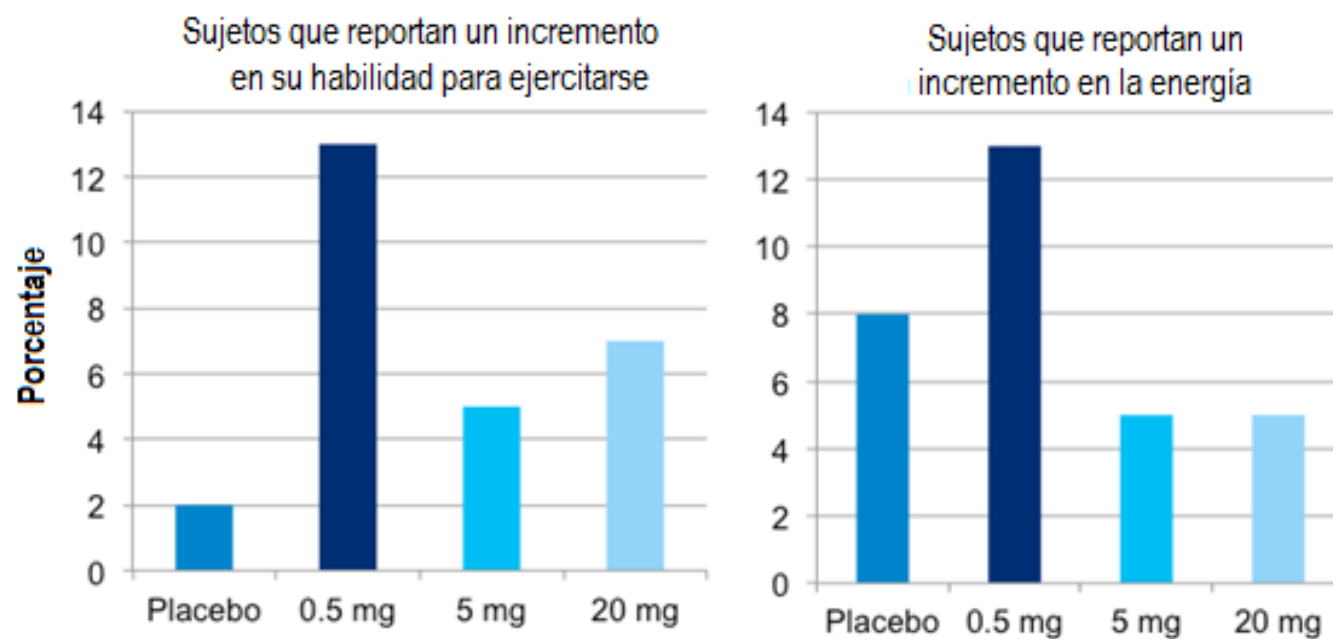
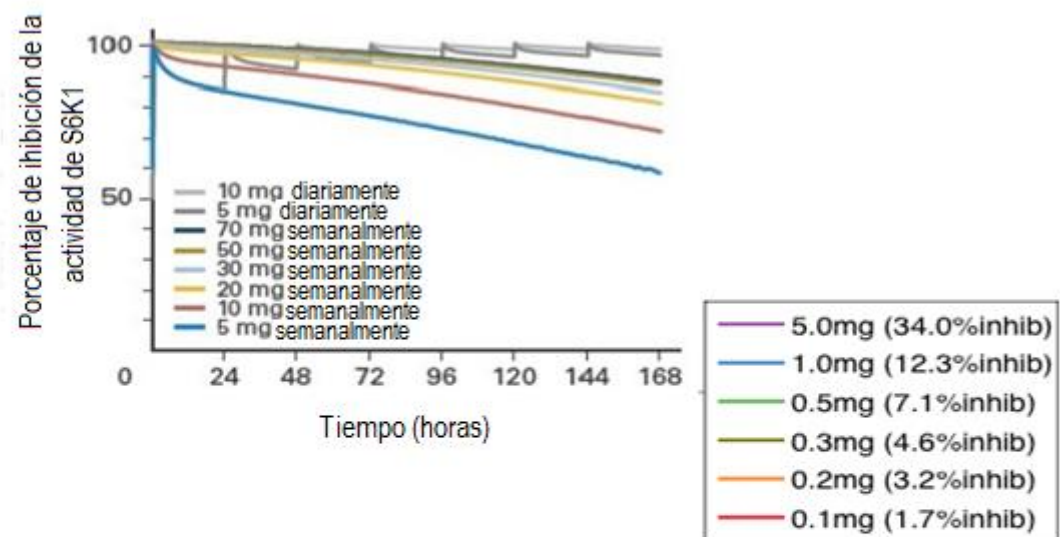


FIG. 47

A.



B.

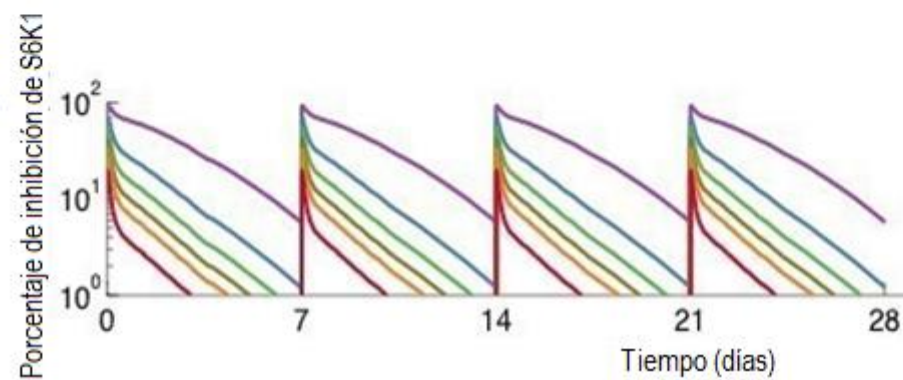


FIG. 48

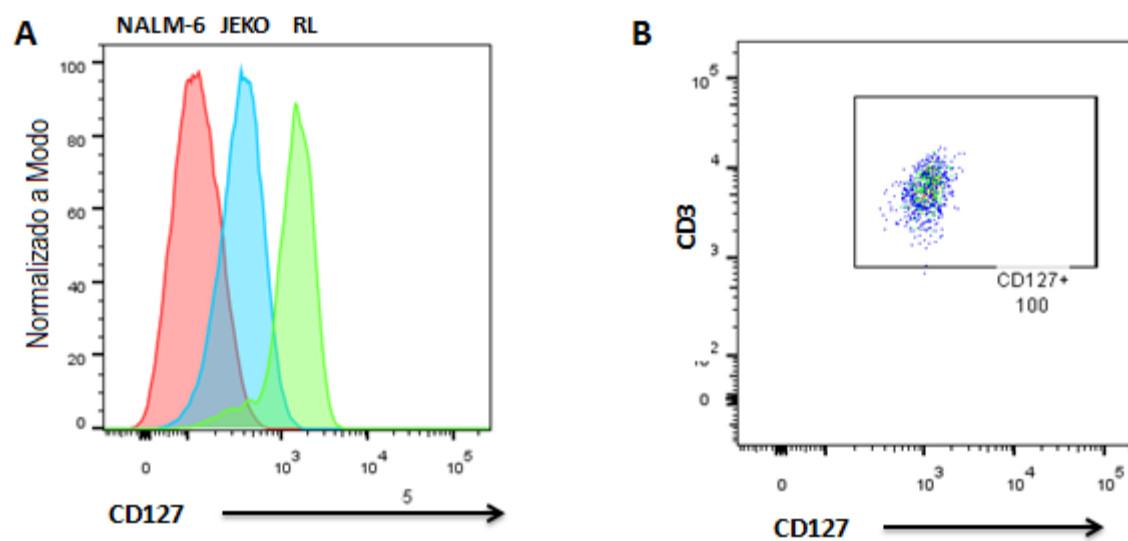


FIG. 49

A

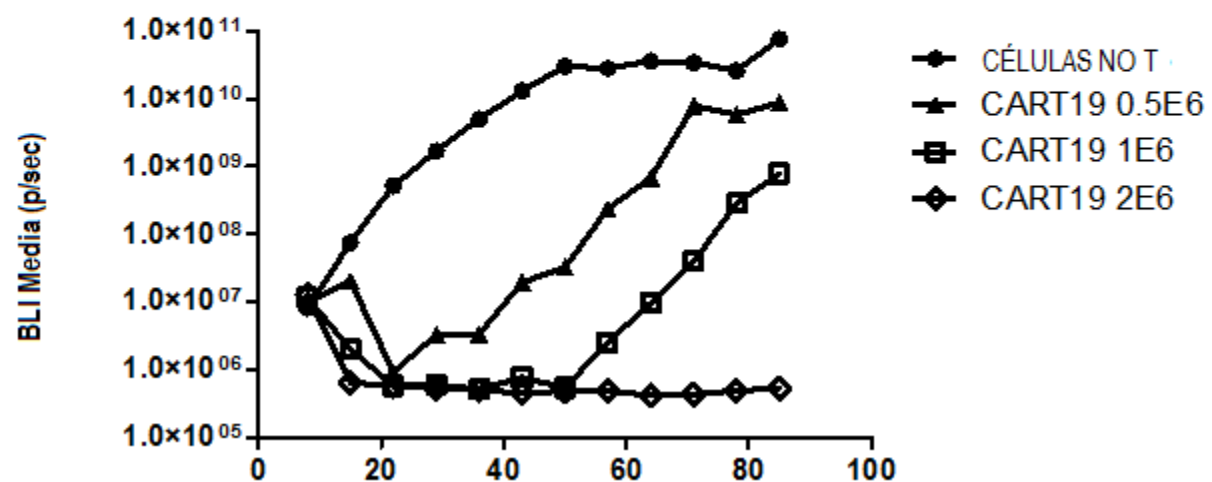
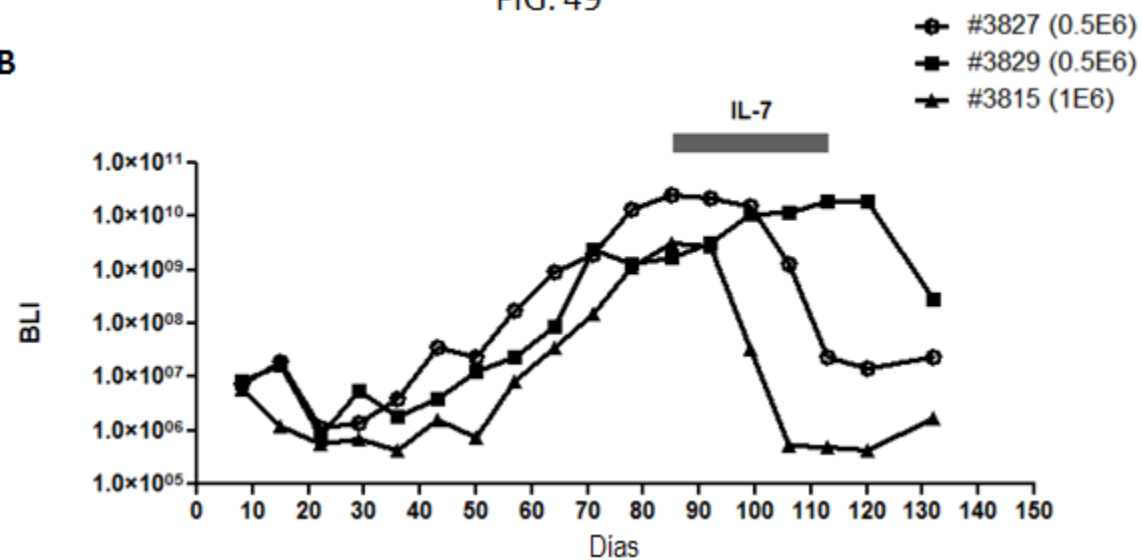


FIG. 49

B



C

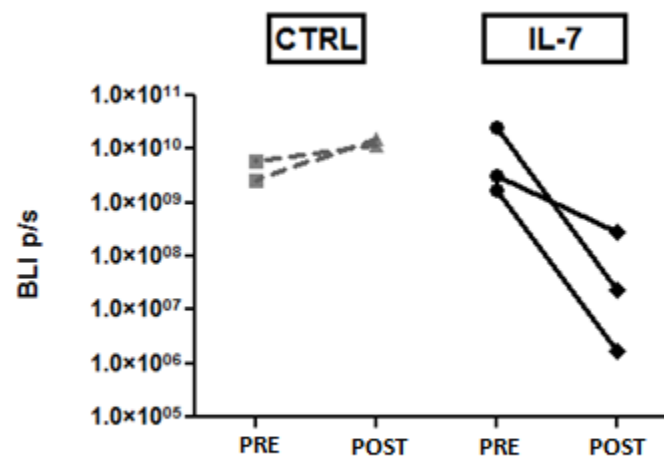


FIG. 50

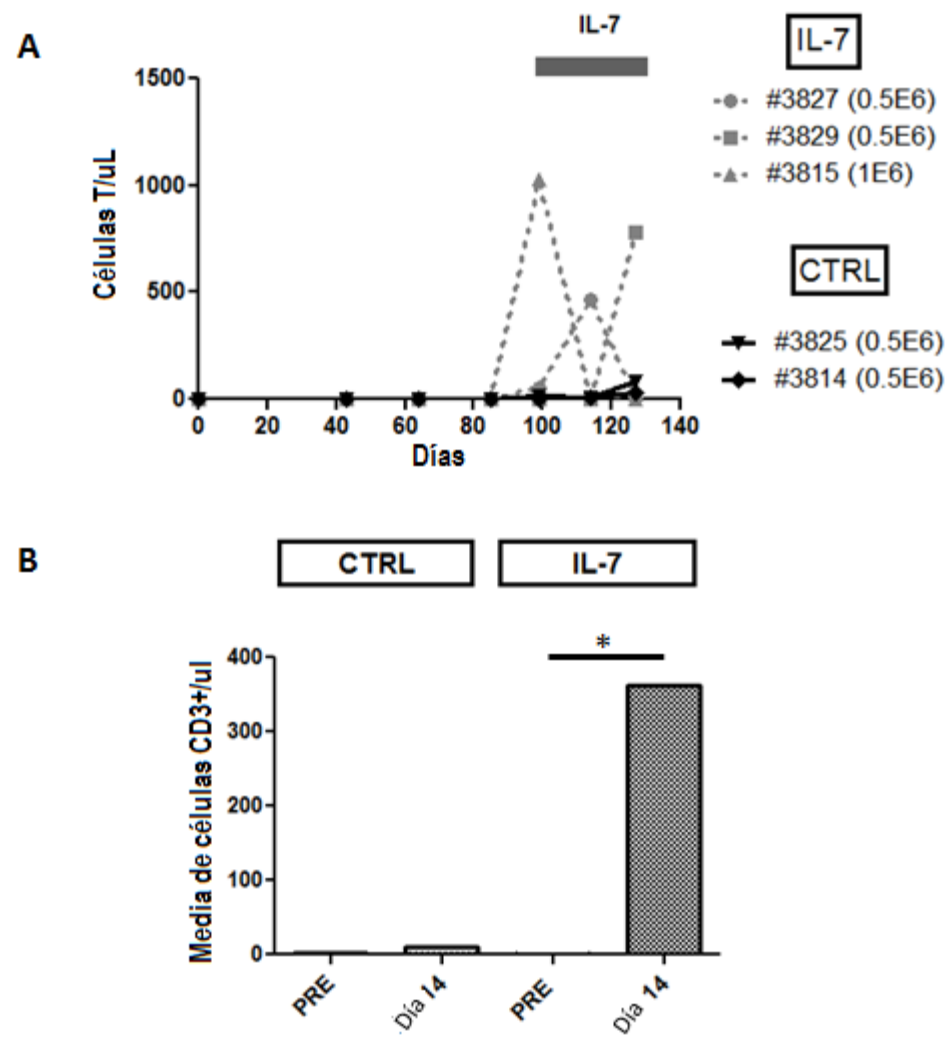


FIG. 51

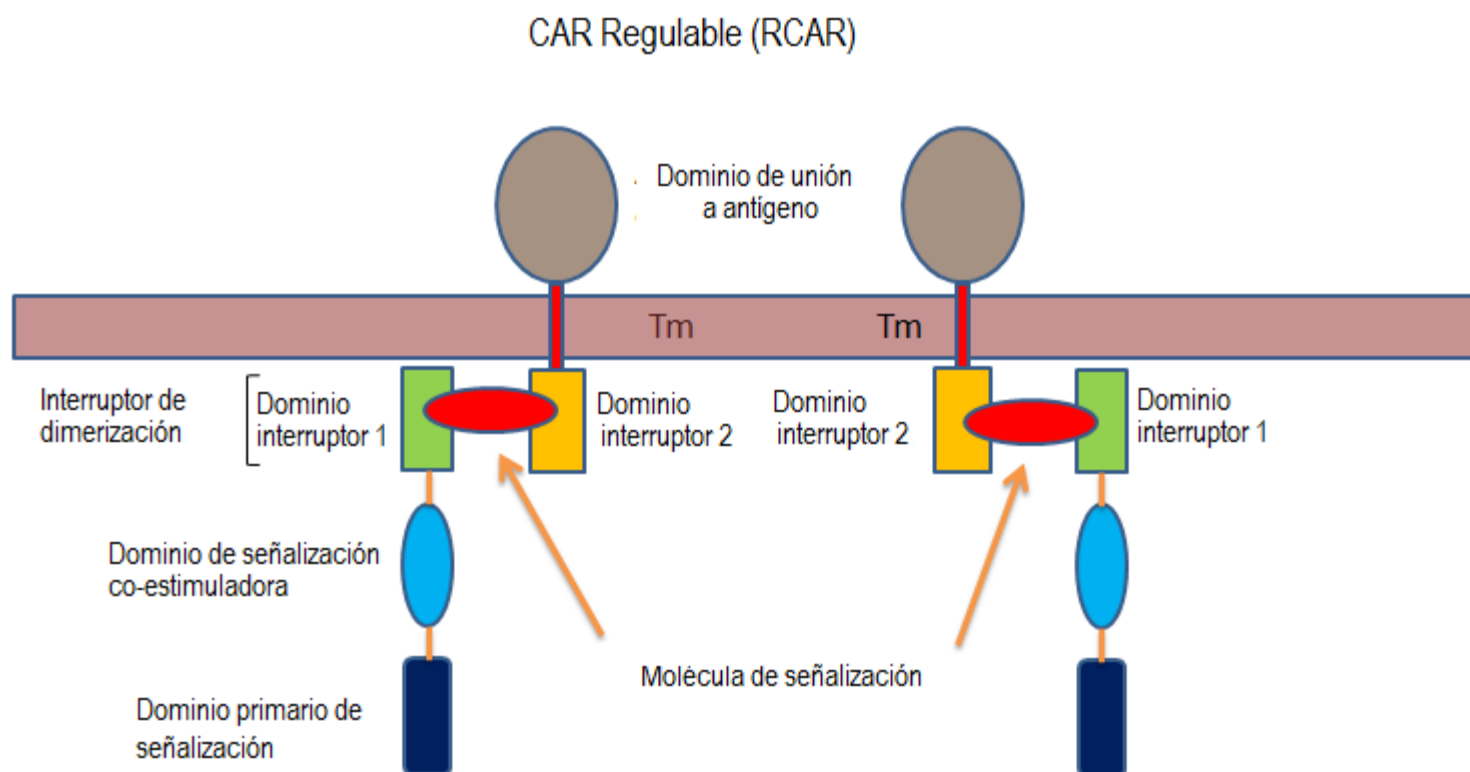


FIG. 52A

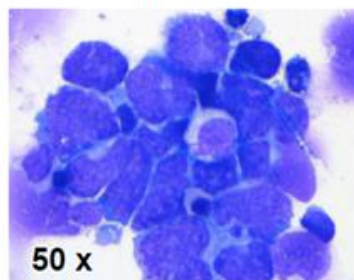


FIG. 52B

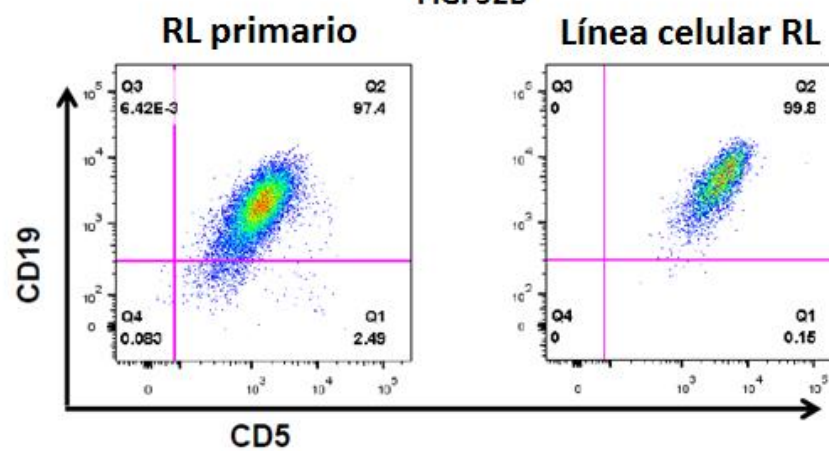


FIG. 52C

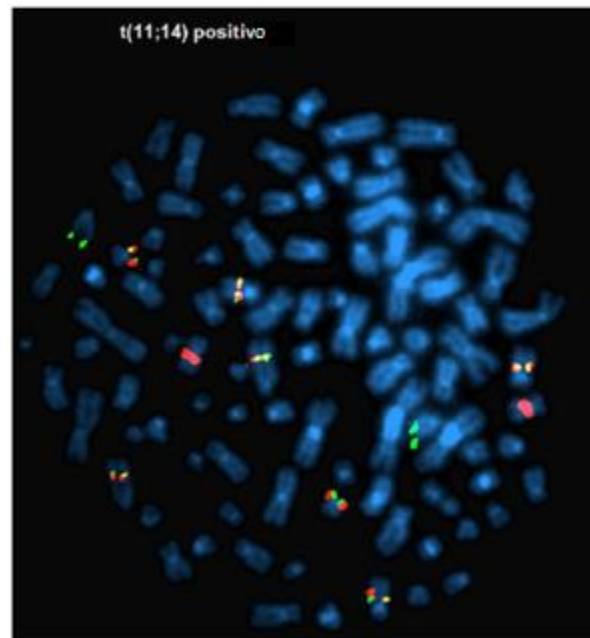


FIG. 52D

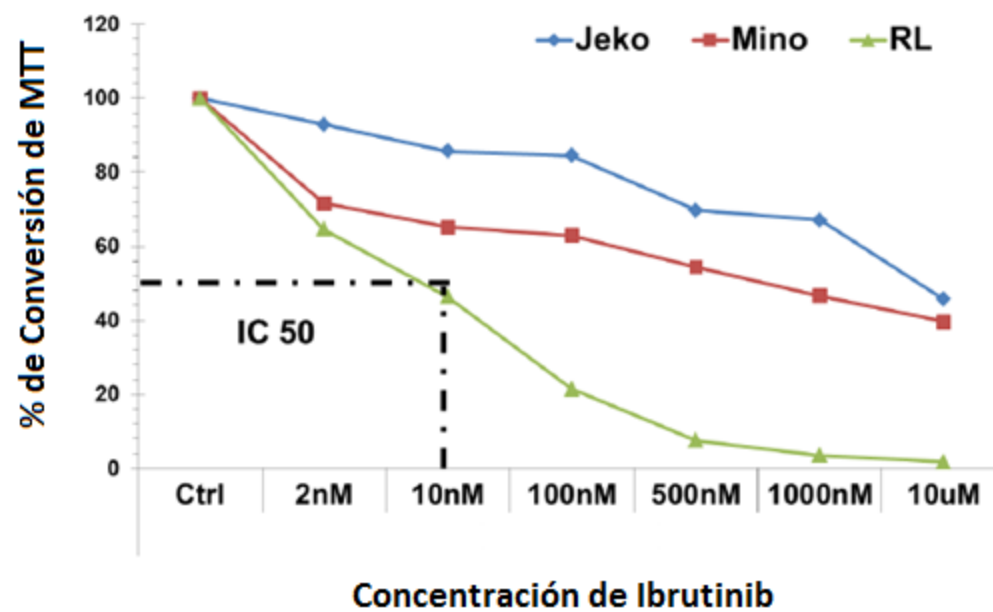


FIG. 52E

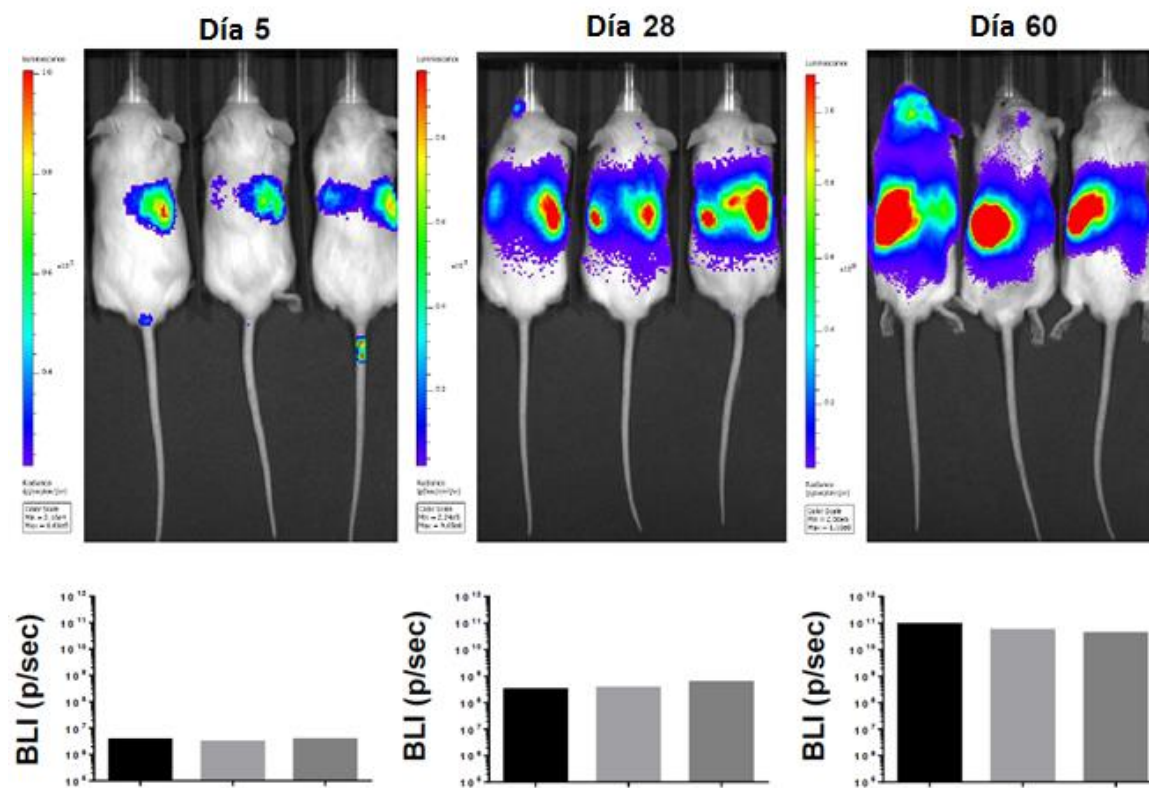
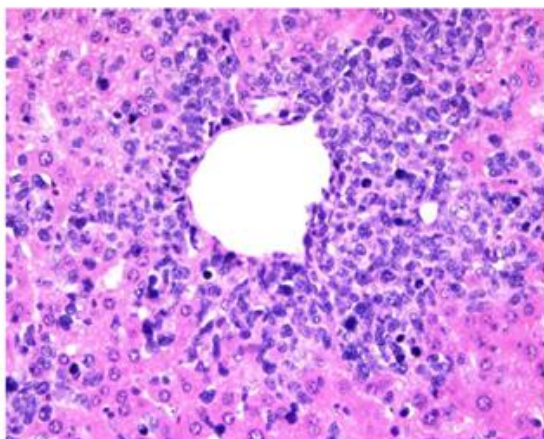
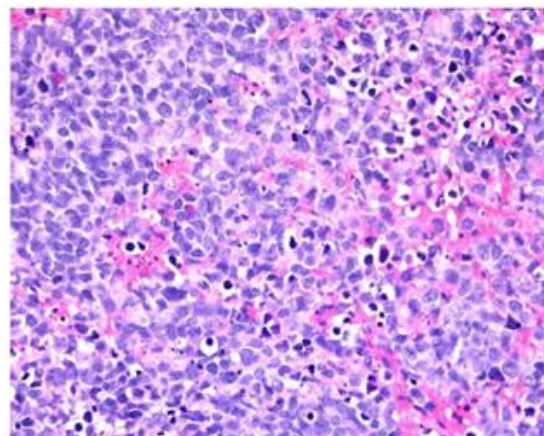


FIG. 52F

LÍNEA CELULAR MCL-RL



HÍGADO



BAZO

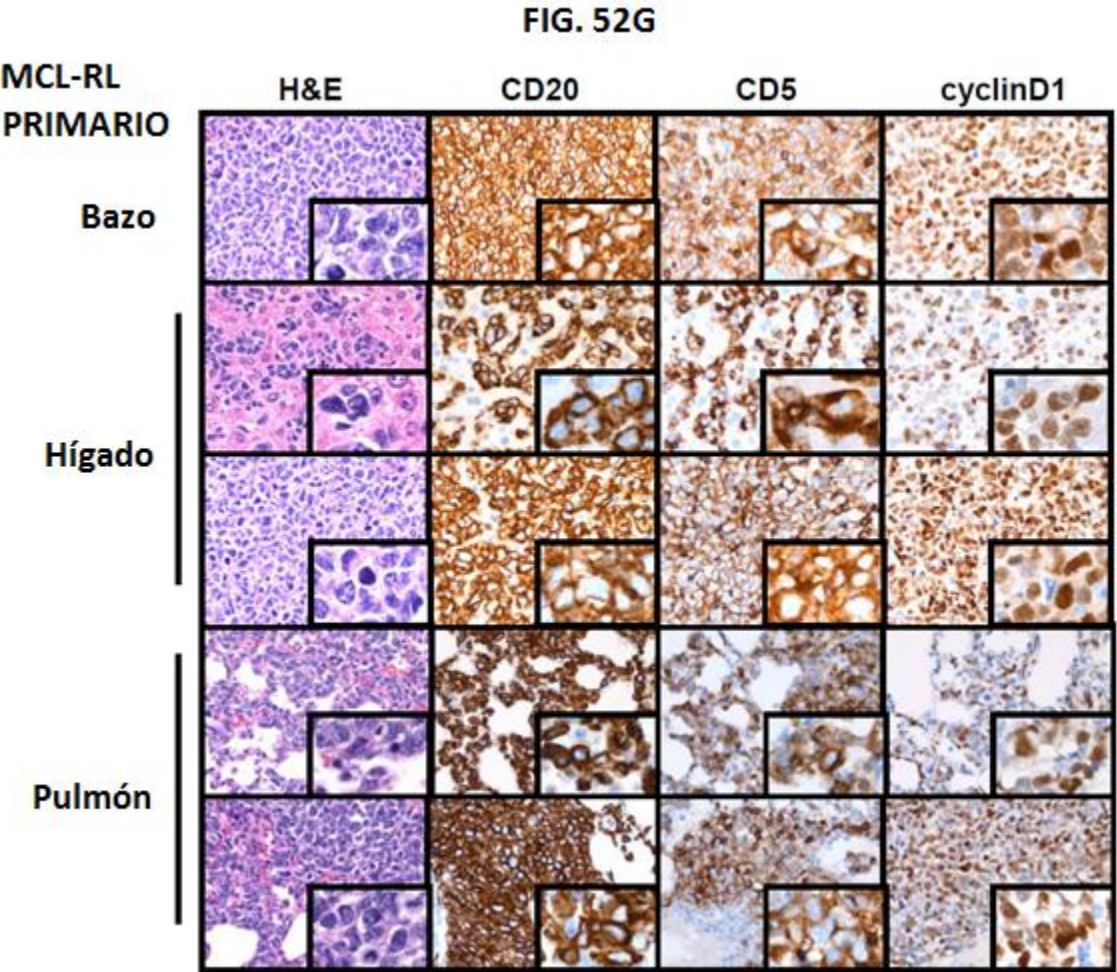
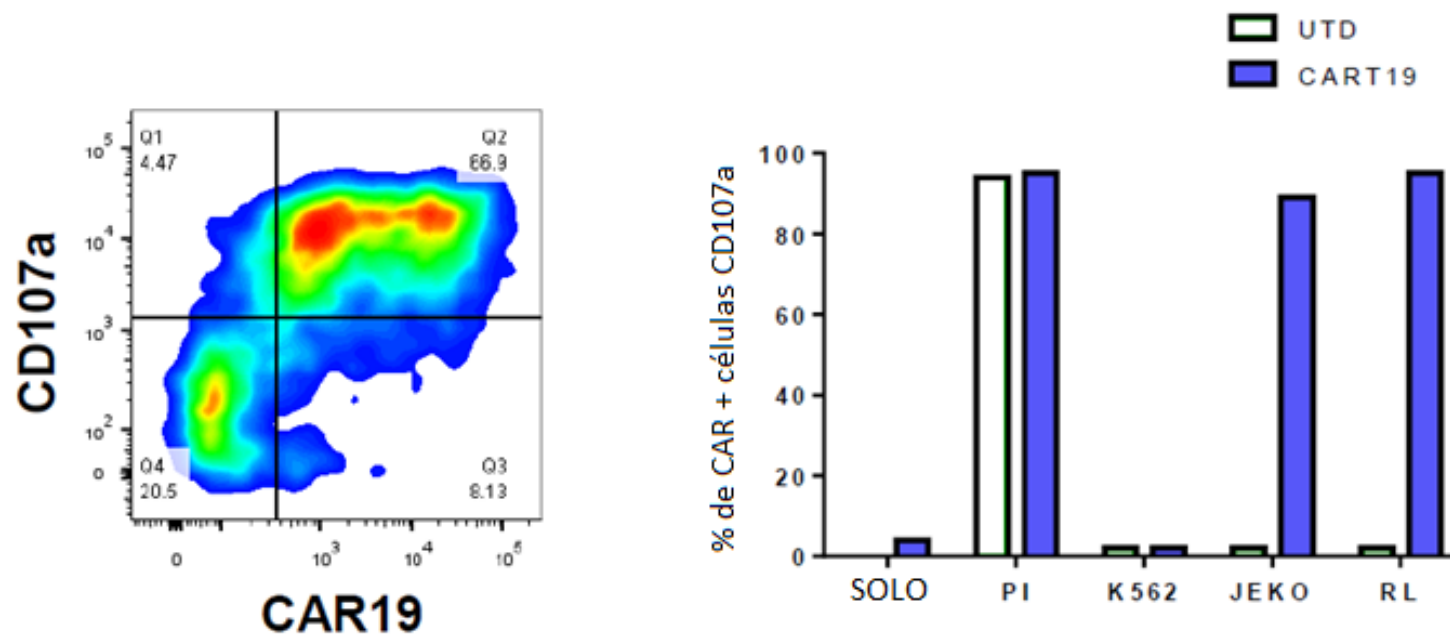


FIG. 53A



FIGS. 53 B y C

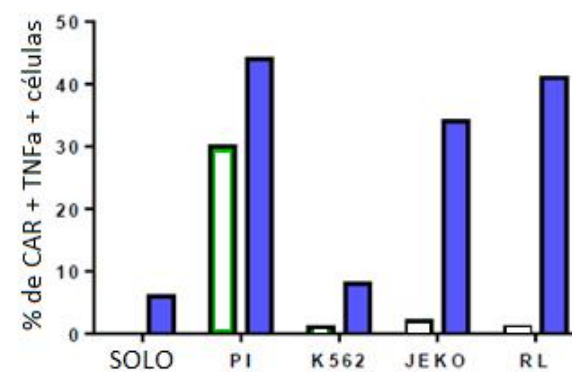
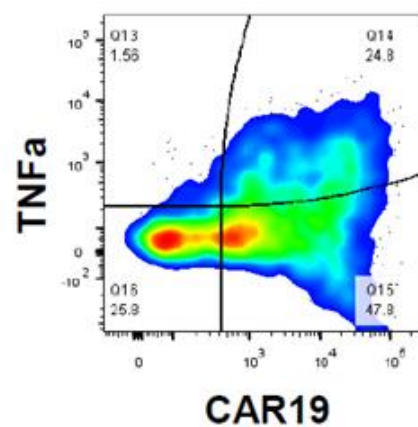
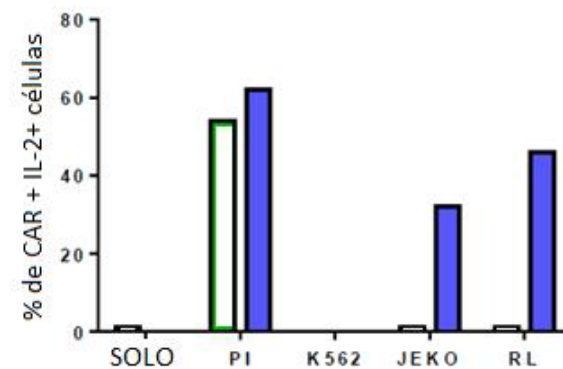
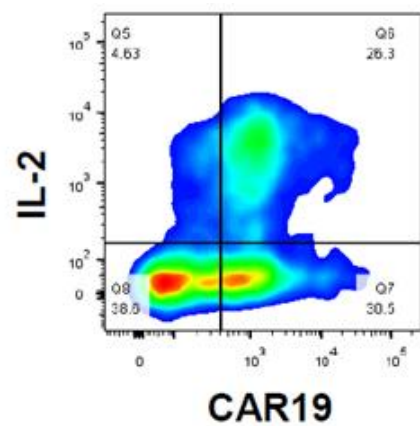


FIG. 53C

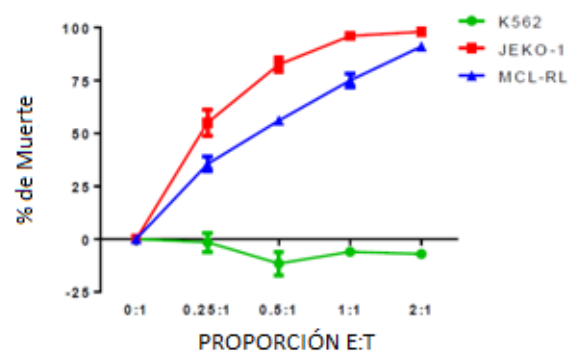


FIG. 53D

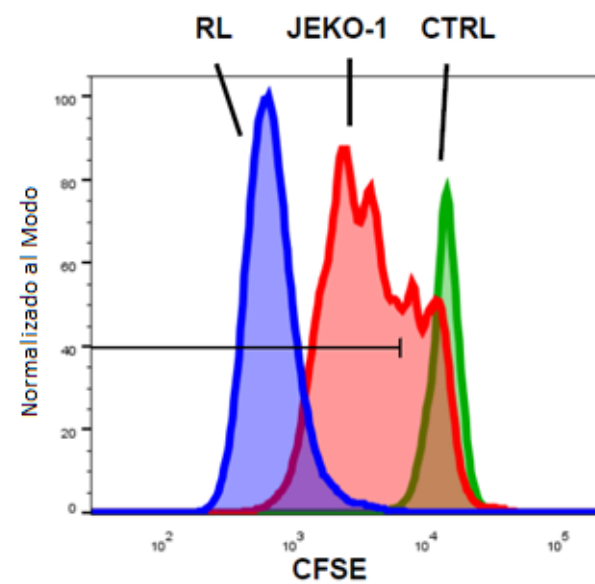


FIG. 53E

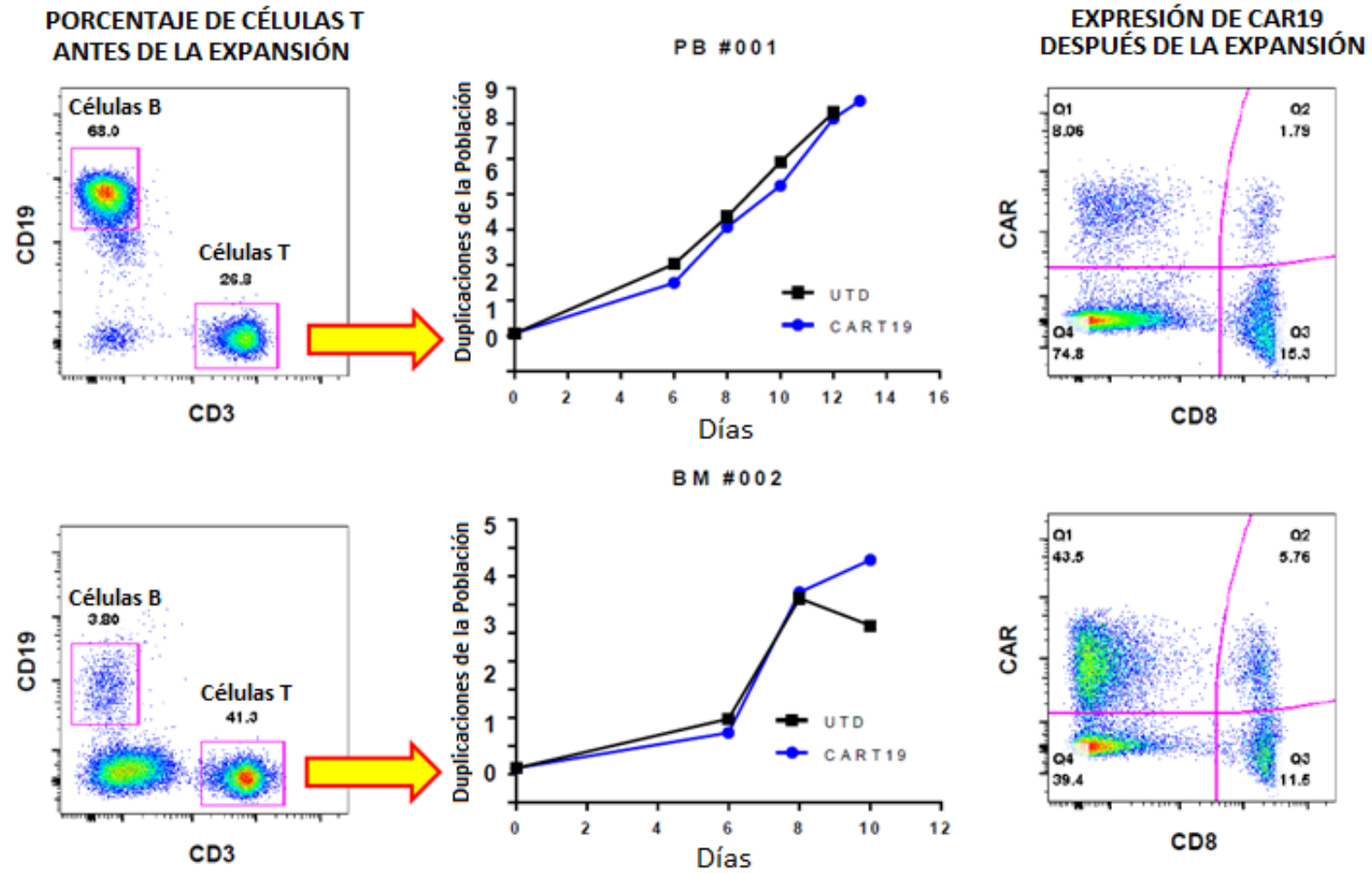


FIG. 53F

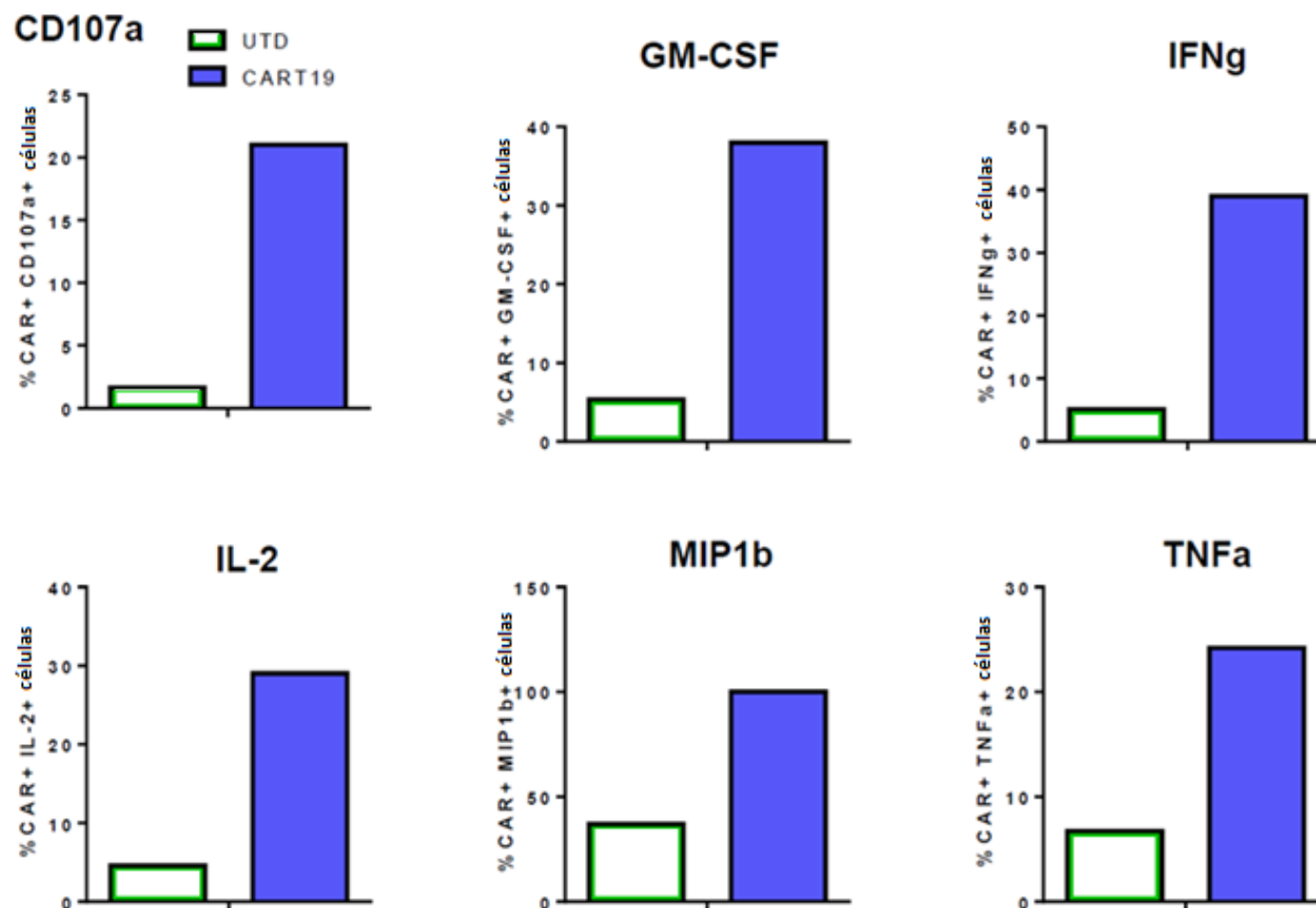


FIG. 54A

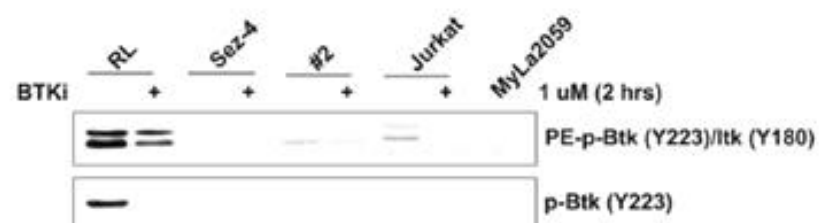
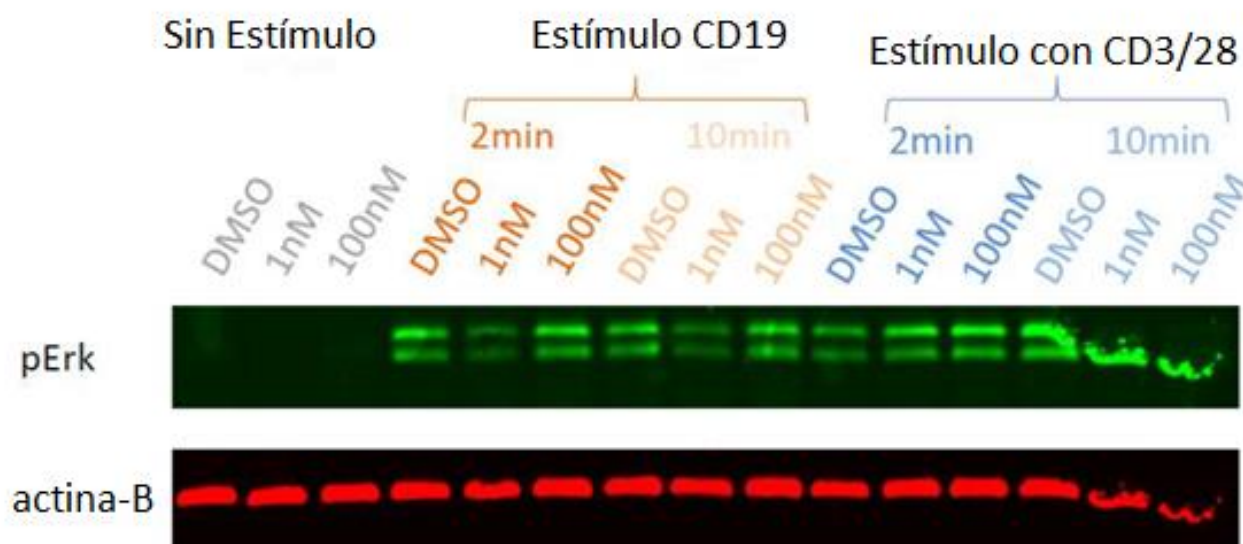


FIG. 54B

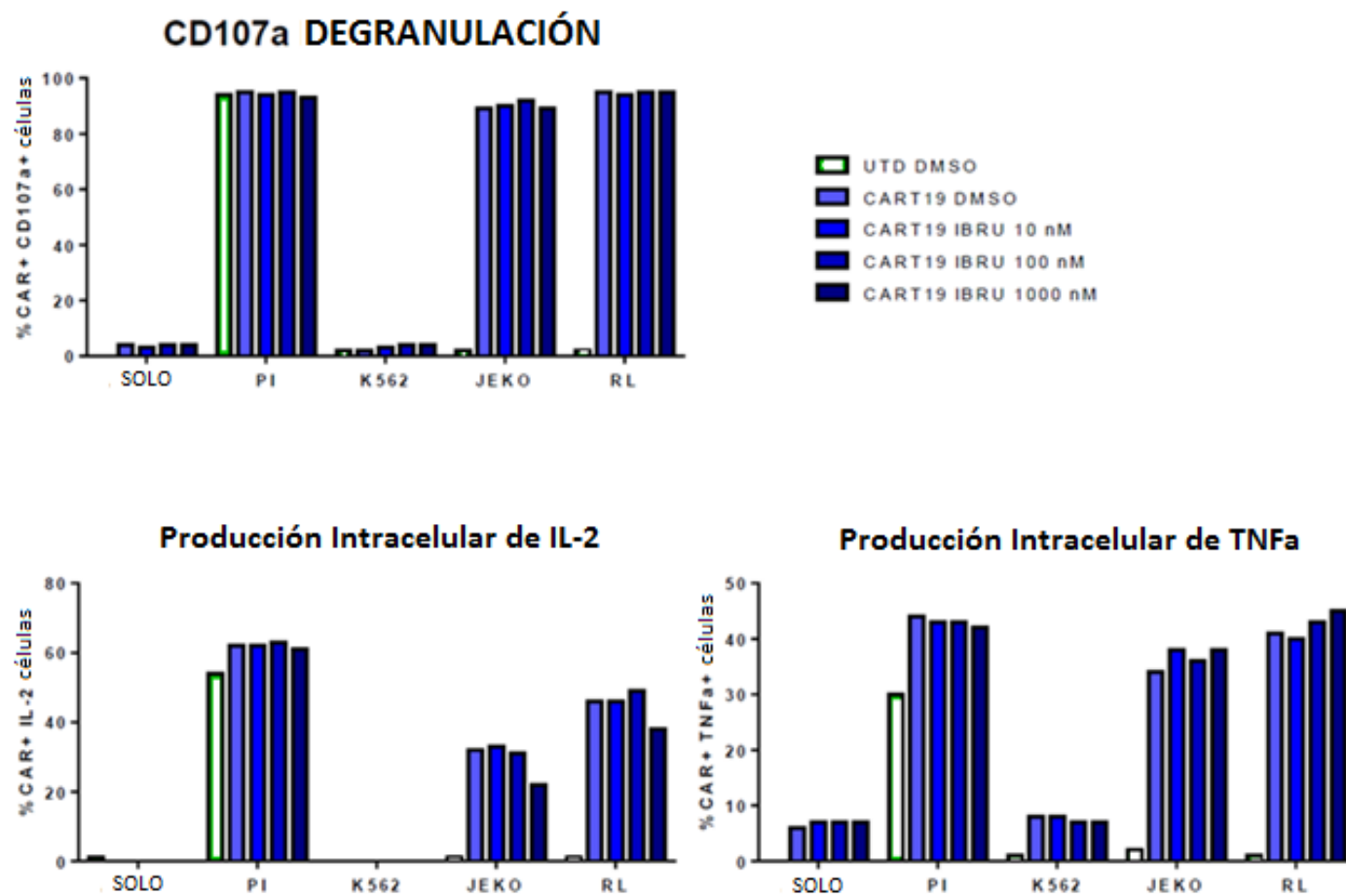


**FIG. 54C**

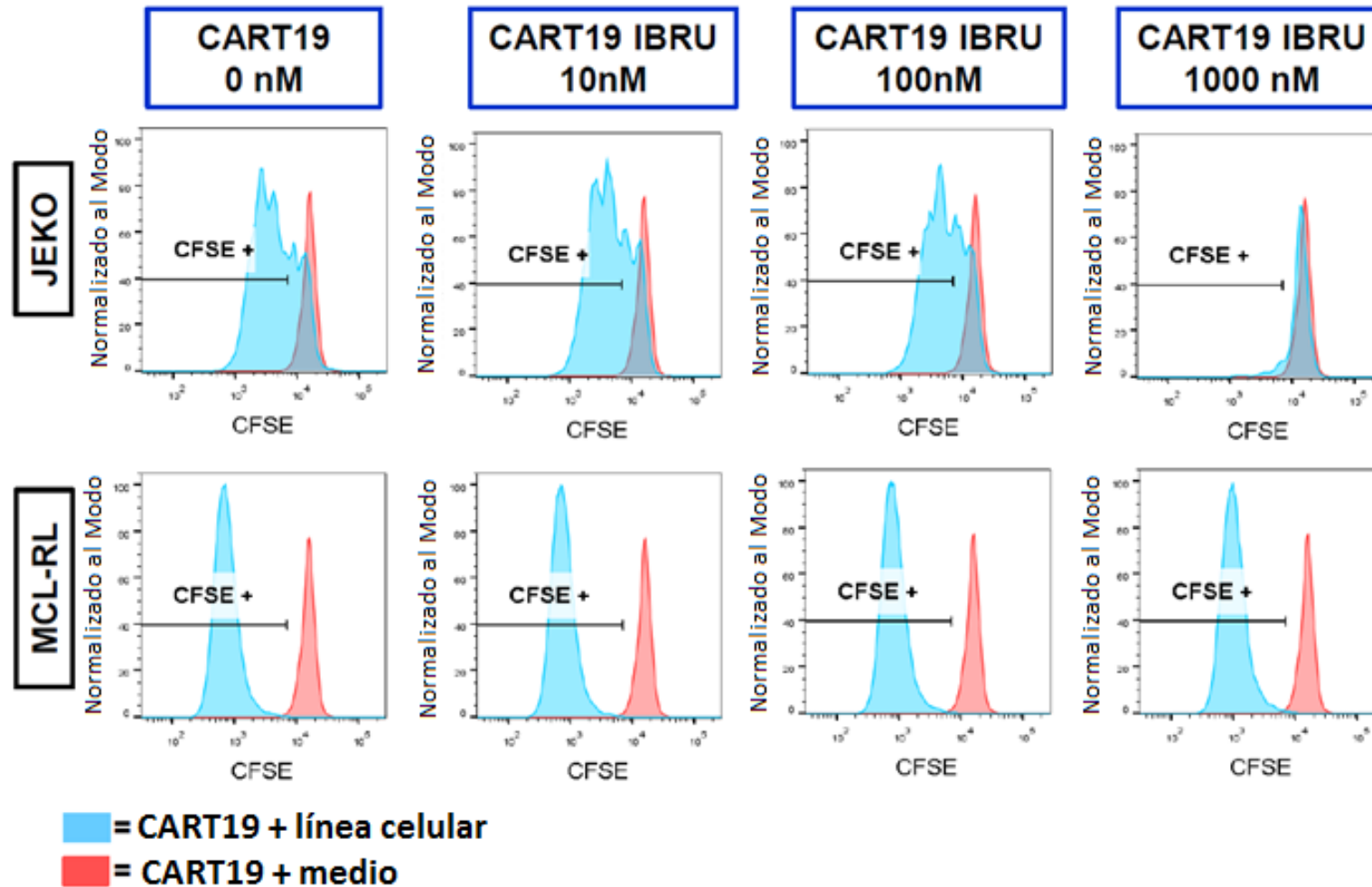


FIG. 54D

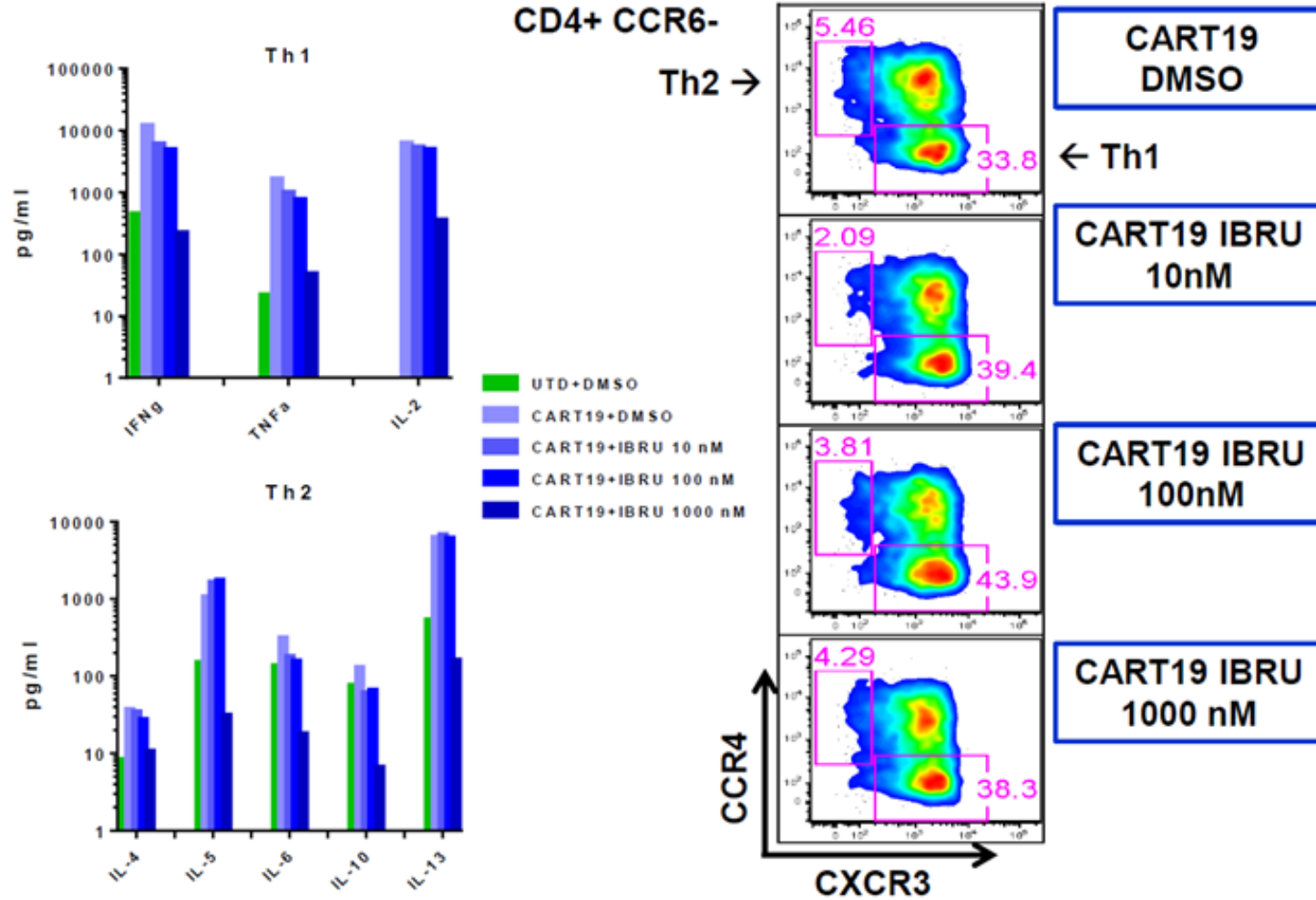


FIG. 54E

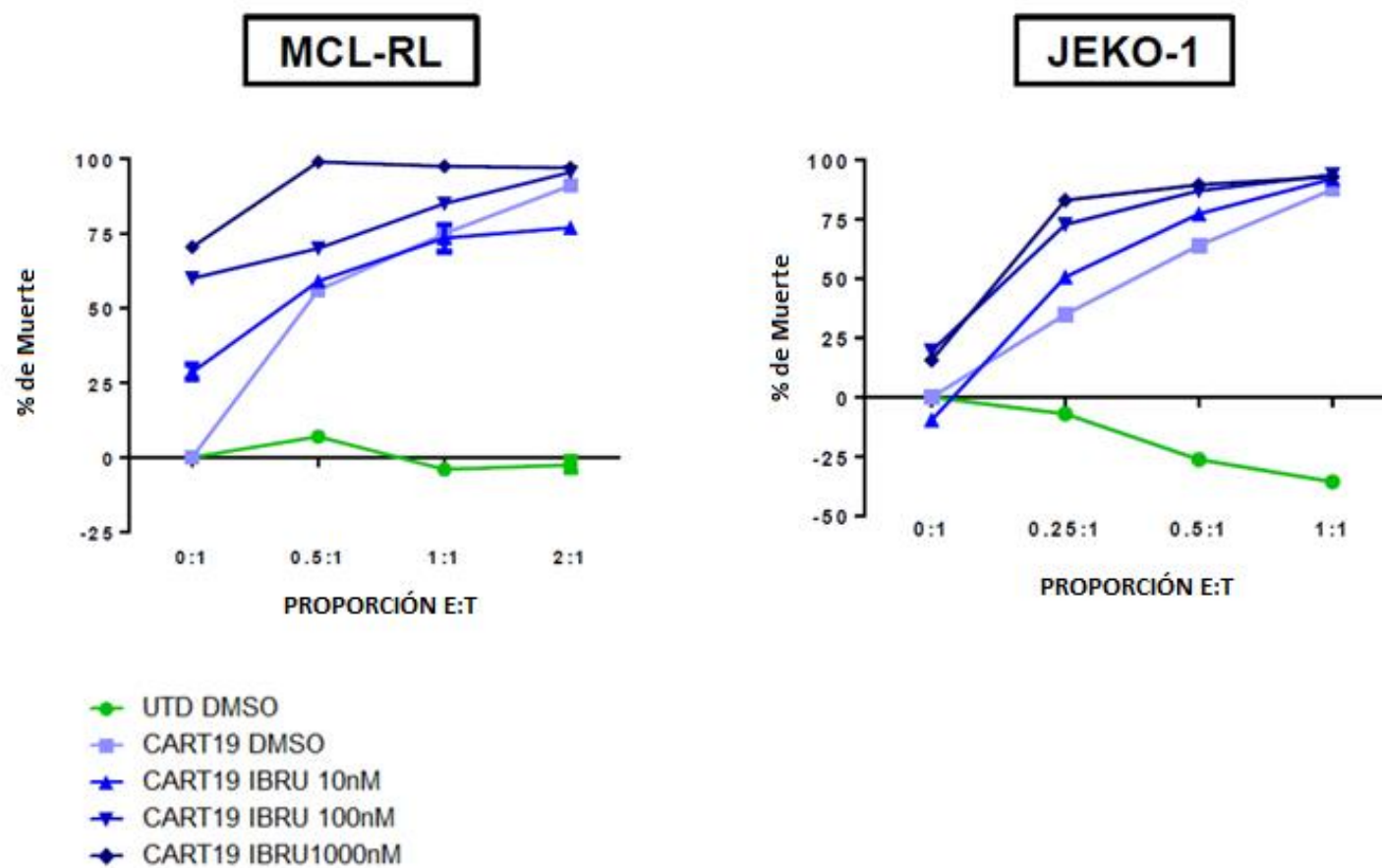
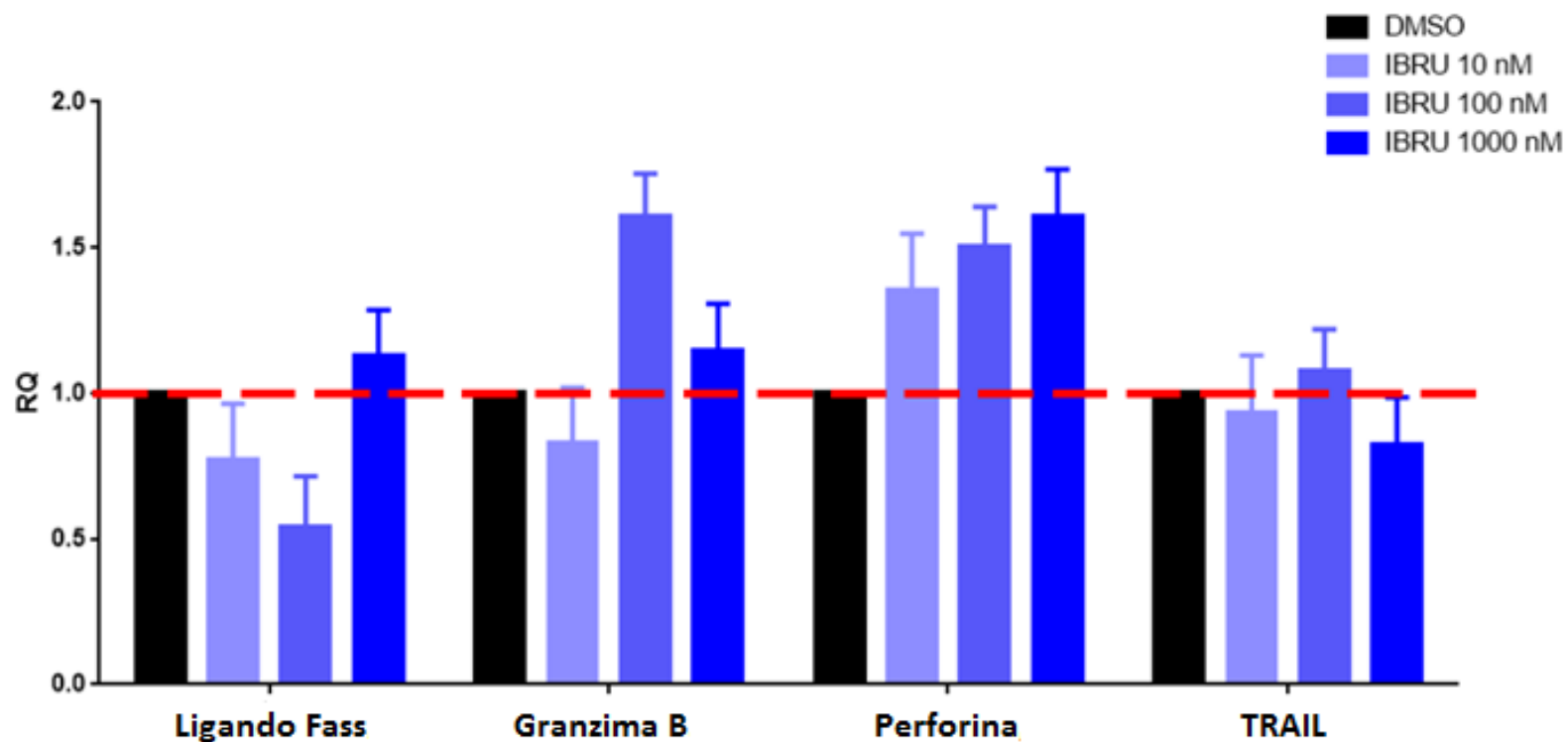


FIG. 54F

DÍA 10 DE EXPANSIÓN DE CART19



Resultados confirmados mediante citometría de flujo.

FIG. 55

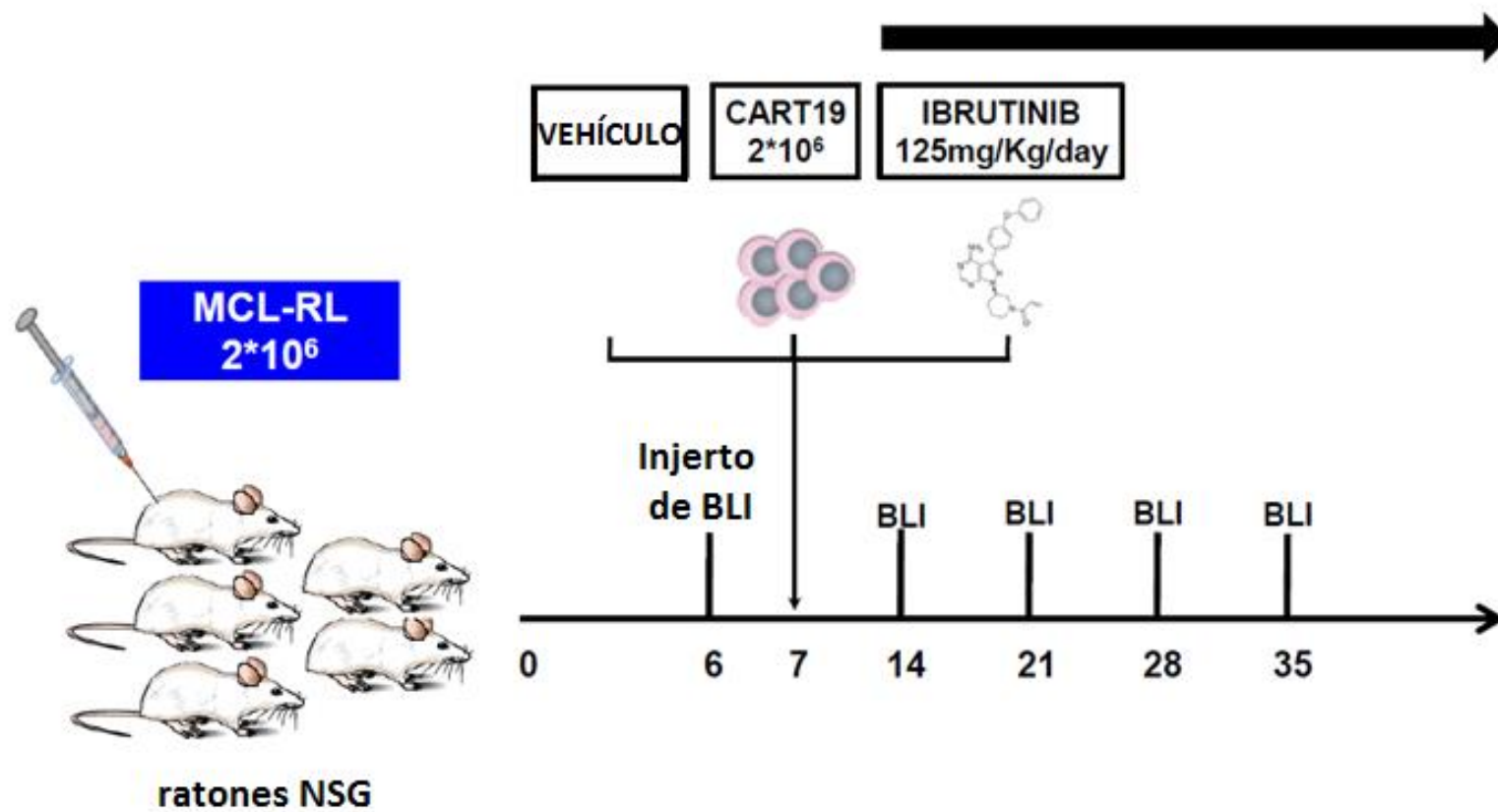


FIG. 56

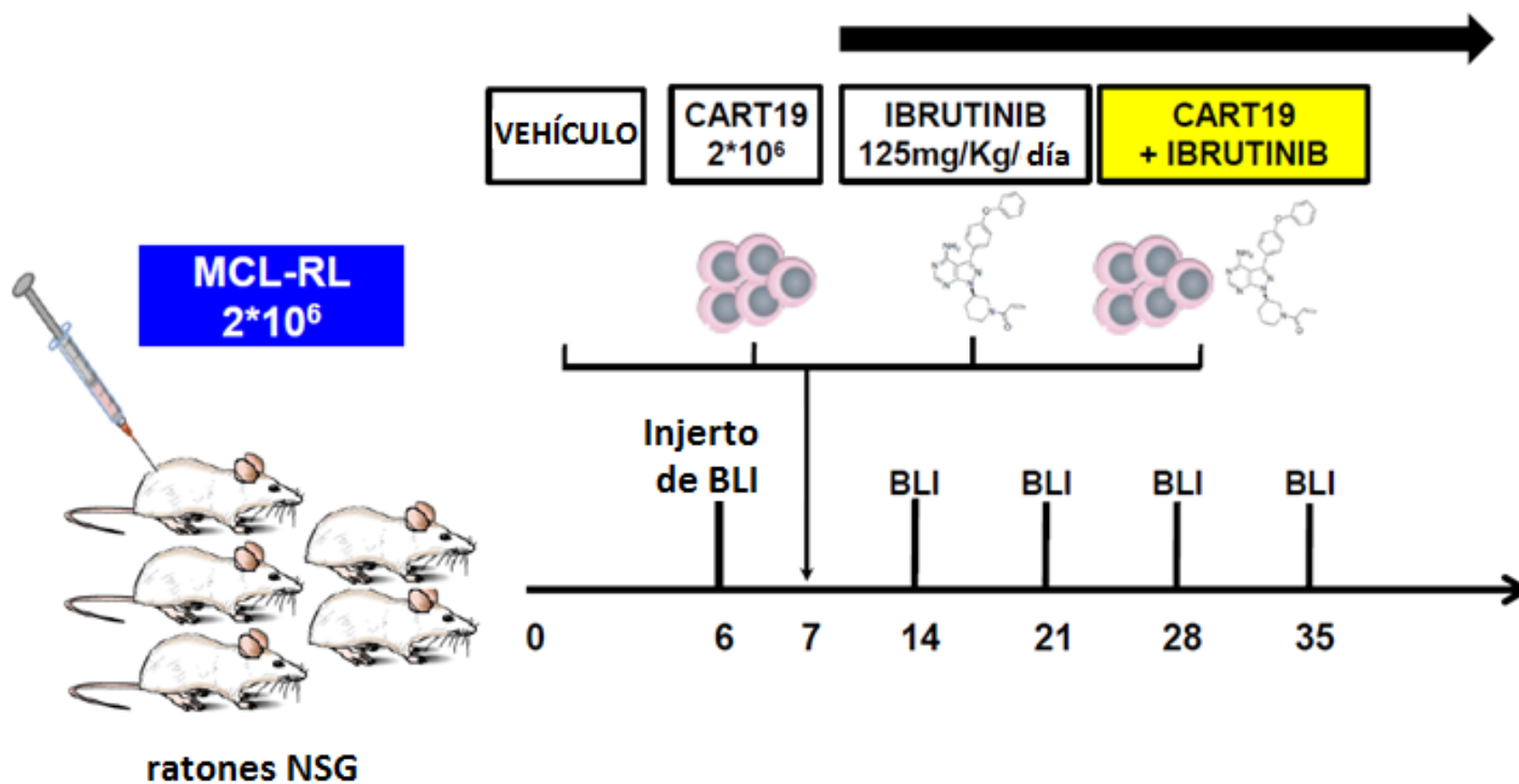
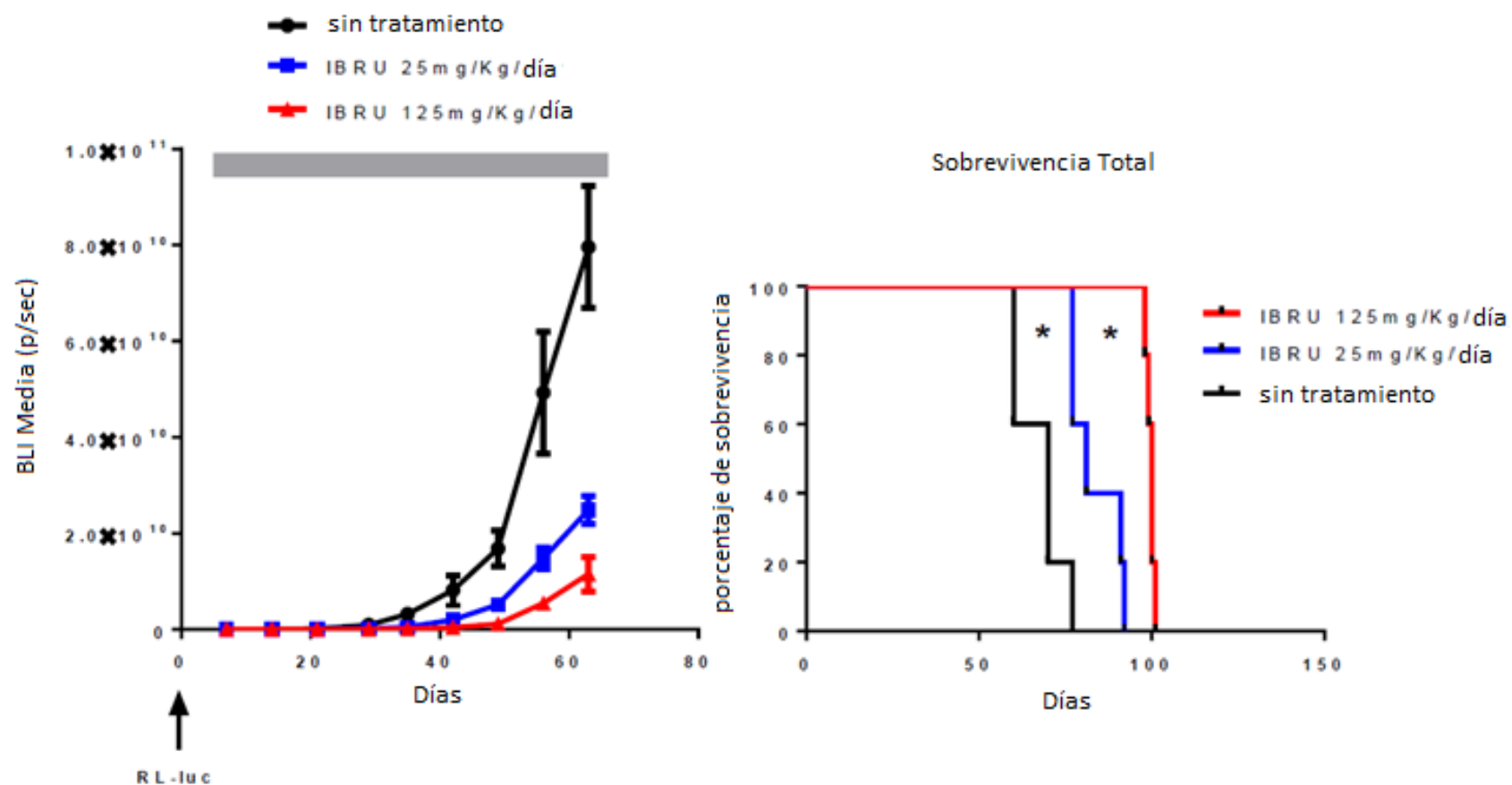
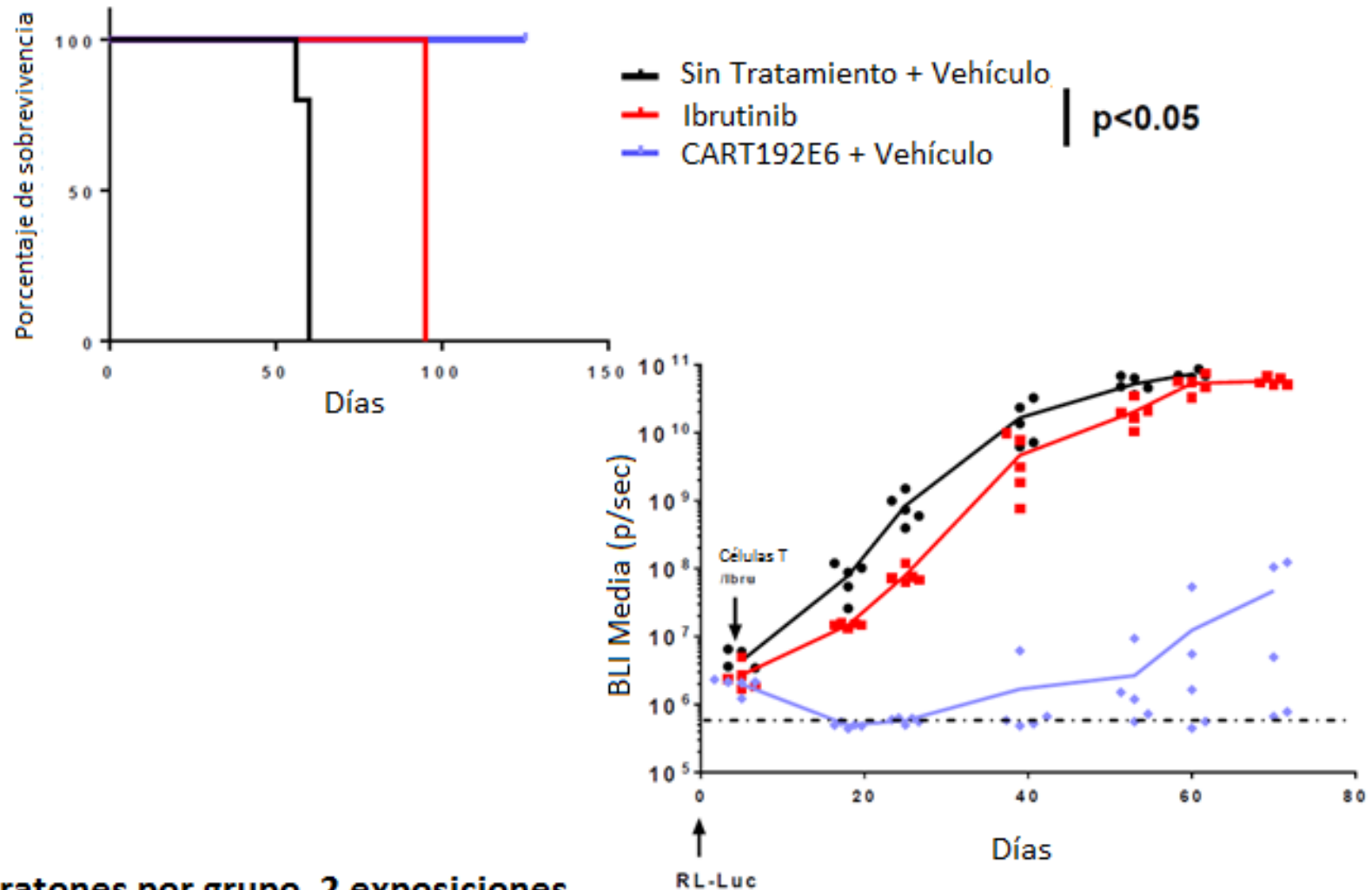


FIG. 57



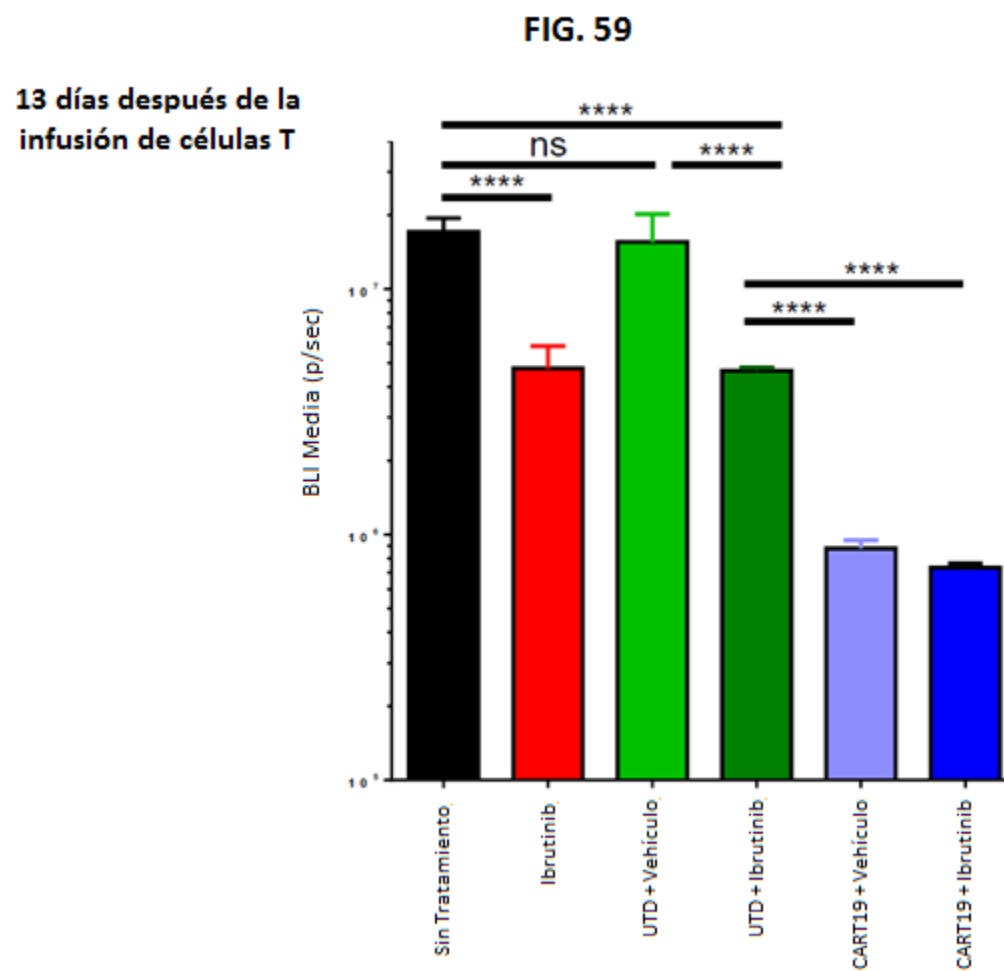
4 ratones por grupo

FIG. 58



5 ratones por grupo, 2 exposiciones

P < 0.05 en todo momento



2 Experimentos, 5 ratones por grupo

FIG. 60

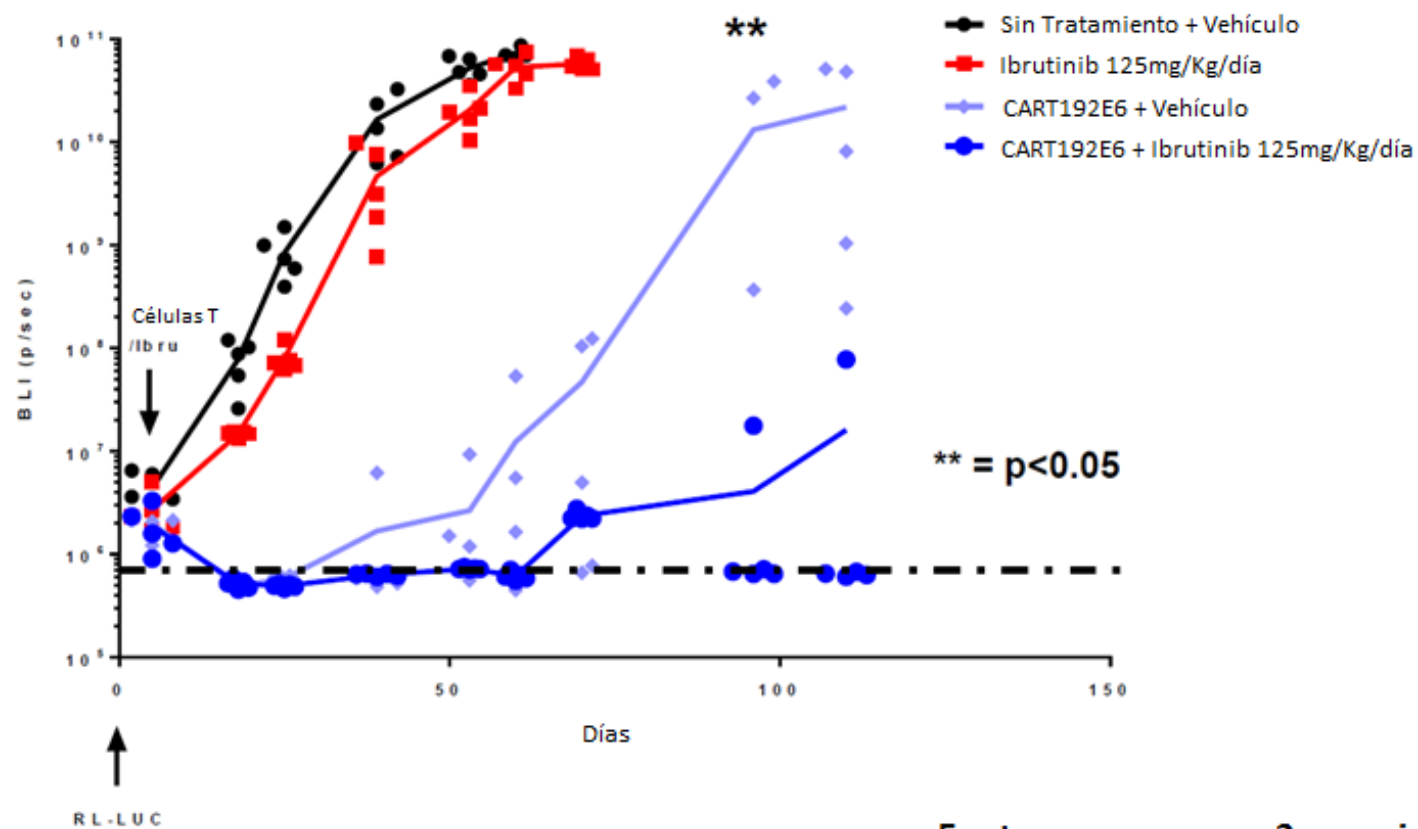


FIG. 61A

## Citoquinas de Th1

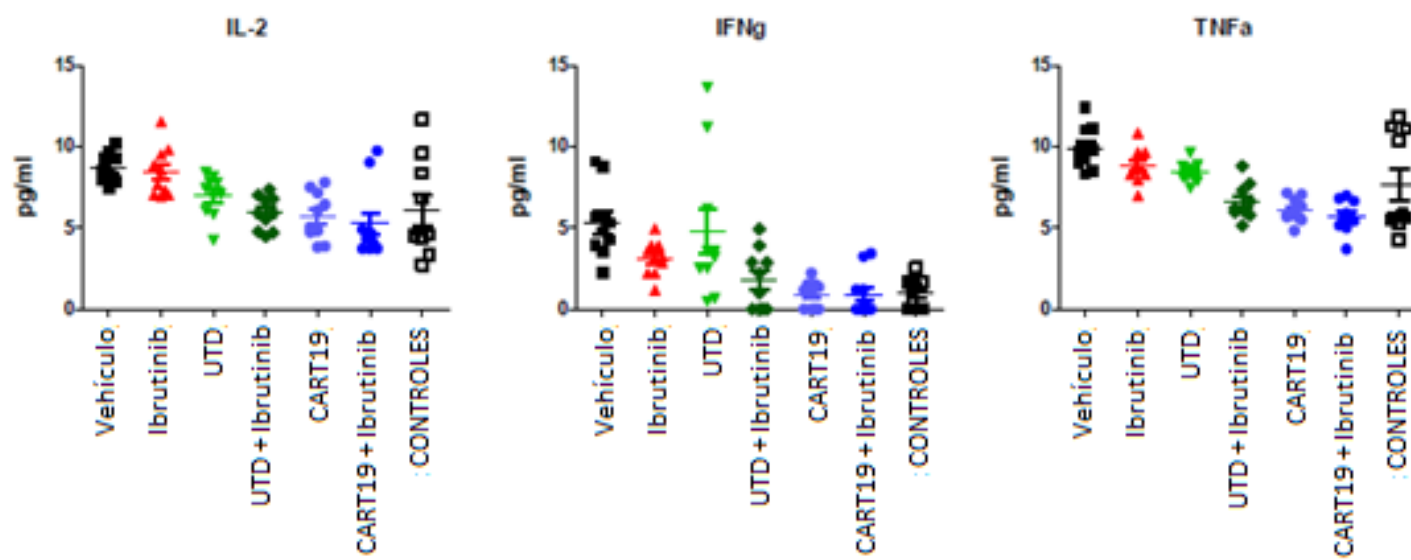
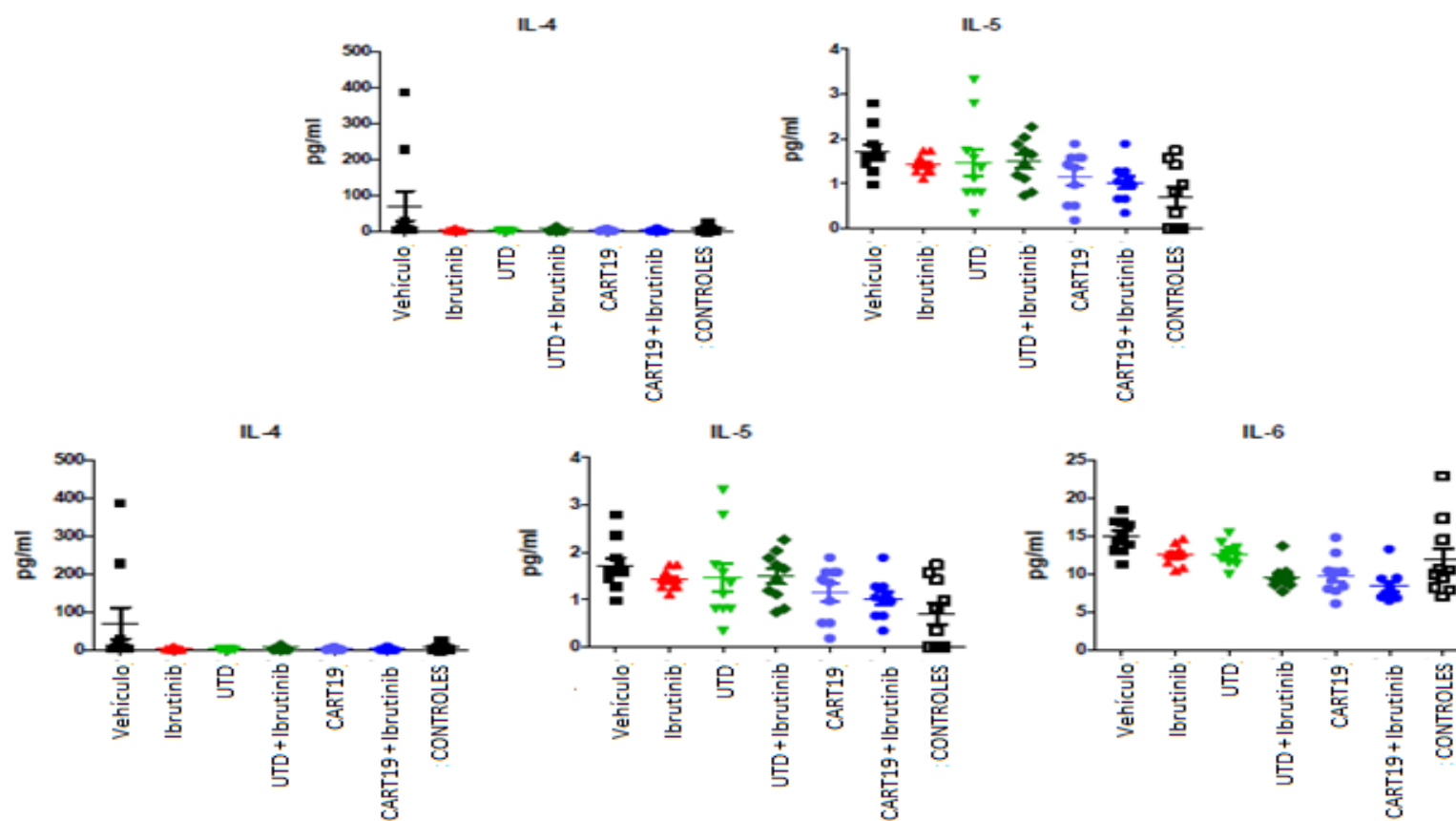
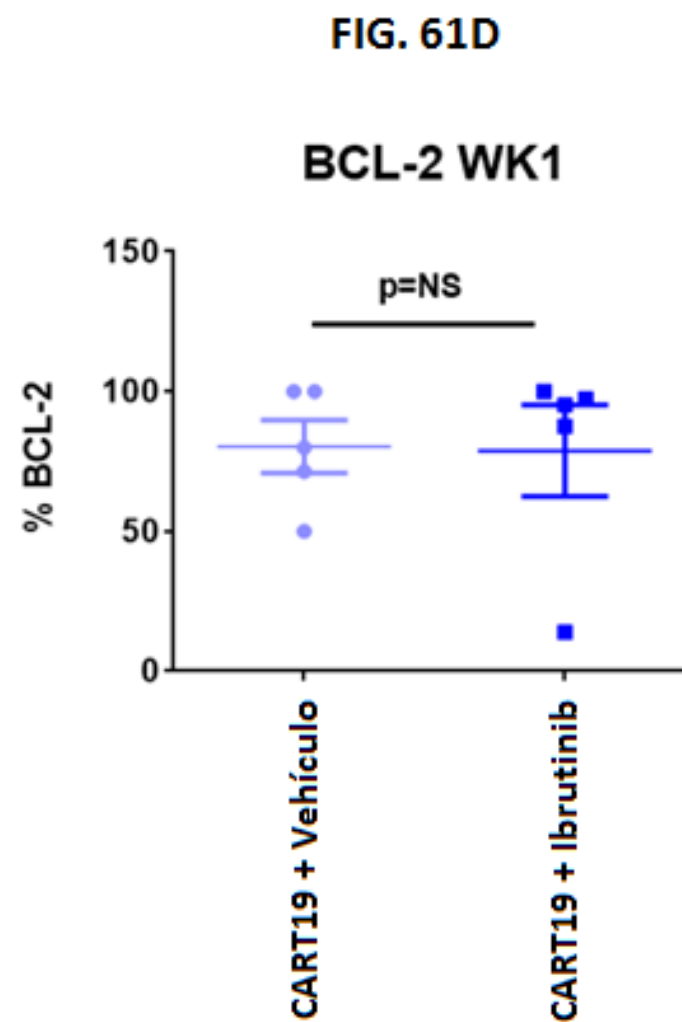
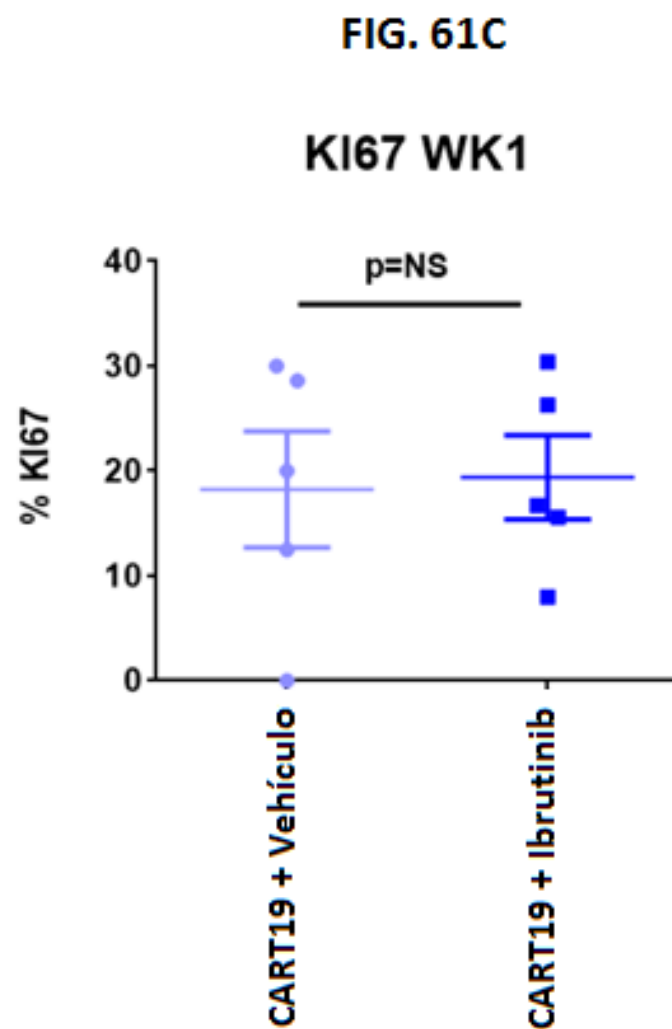


FIG. 61B

## Citoquinas de Th2





Células PB T, 1 semana después de la infusión.