

How are we helping patients under economic restrictions: the Cuban experience

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Topics

- Health System in Cuba.
- Cancer in Cuba & Cuban Program for Cancer Control
- Cuban Biotech industry & Center of Molecular Immunology

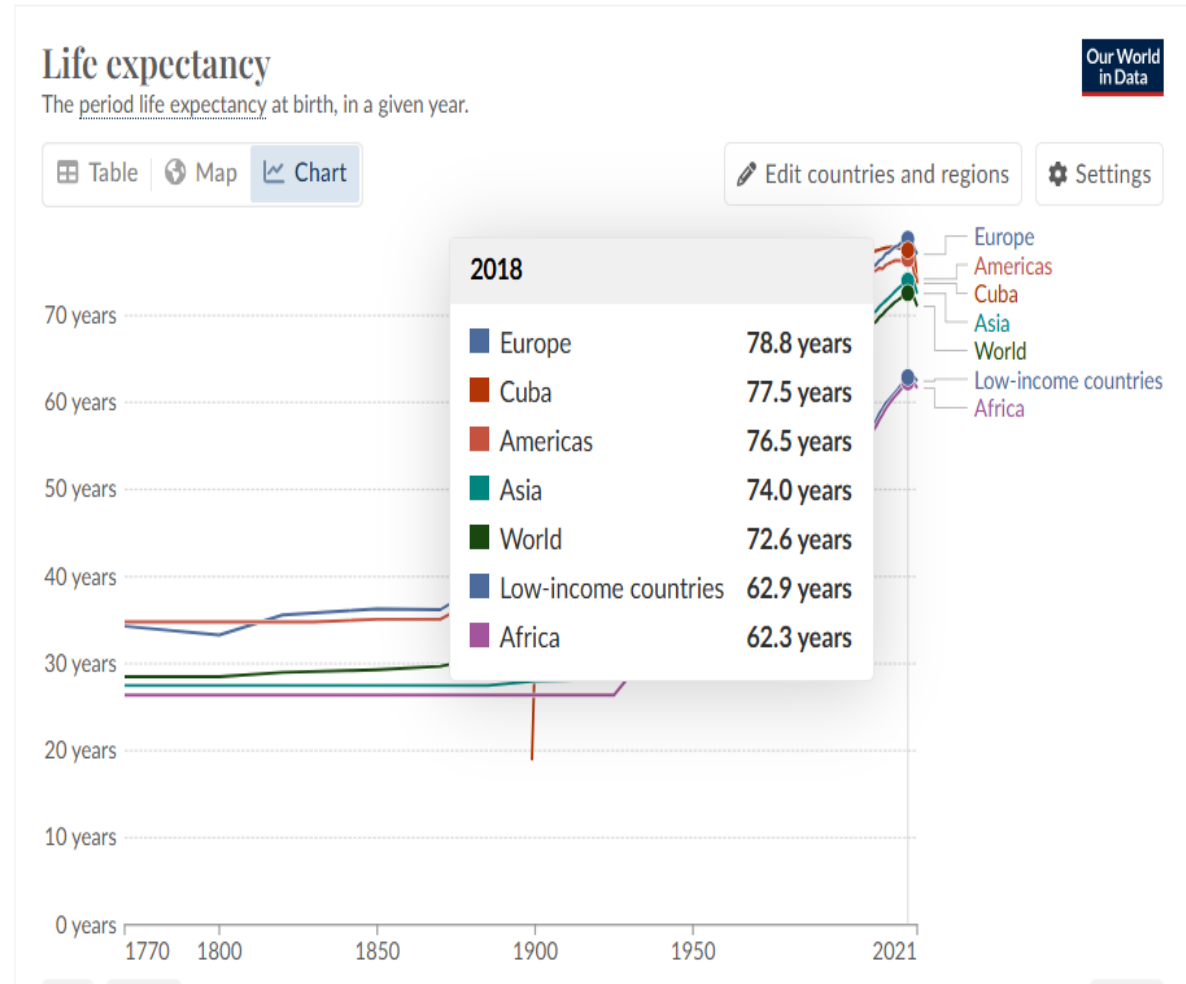
HEALTH SYSTEM IN CUBA

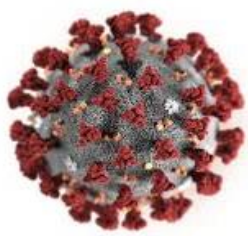
Science and Challenges for Cuban Public Health in the 21st Century

- Universal health coverage and free medical attention.
- Health System based on the primary care attention, oriented to disease prevention.
- Cuba's physician–population ratio (79/10 000), is among the highest in the world.
- Infant mortality in 2023 was 7 per 1000 live births vs 26, in the ROW
- The country has eliminated 14 infectious diseases
- Cuba was certified by WHO as the first country to eliminate mother-to-child transmission of HIV and syphilis, in 2015.

Population &
Demography Data
Explorer

Our World
in Data





COVID-19 immunization in Cuba



Ensayo clínico Fase III

Vacunados 1ra dosis:

 **Abdala**

48000

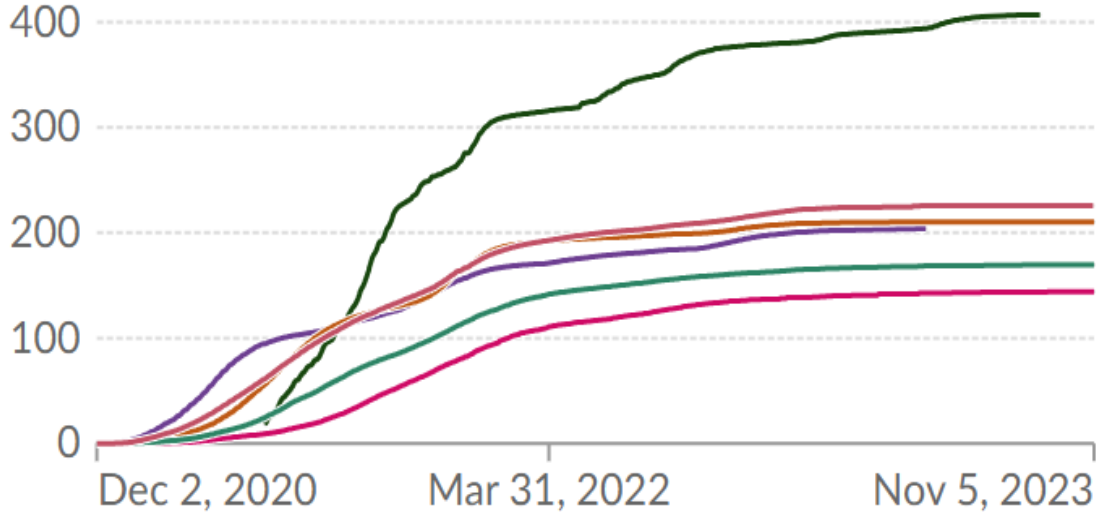
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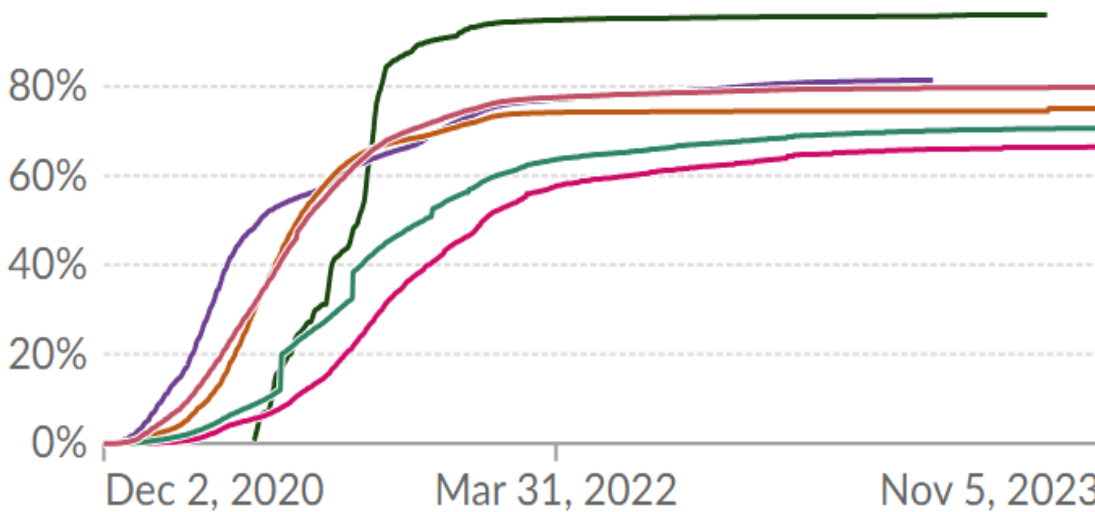
COVID-19 vaccine doses, people with at least one dose, people with a full initial protocol, and boosters per 100 people

High income World European Union United States Lower middle income Cuba

Vaccine doses (per 100)



Share of people with at least one dose



Sep 8, 2023	
Cuba	406.90
High income	225.49
European Union	210.15
World	169.45
Lower middle income	143.89

Sep 8, 2023	
Cuba	96.05%
High income	79.65%
European Union	74.49%
World	70.49%
Lower middle income	66.34%
Low income	32.79%

CANCER



1 in 4 deaths in Cuba is due to cancer

Cuba



Cuban Population: 10 242 351

Cancer is the second leading cause of death

	Deaths	Crude rate	Adjusted rate
Heart disease	32 105	313.5	124.5
Malignant tumors	25 199	246.0	110.6
Cerebrovascular diseases	11 222	109.6	43.7
Influenza and pneumonia	9 200	89.8	35.6
Accidents	5 818	56.8	27.5
Chronic diseases of the respiratory tract lower respiratory	3 930	38.4	16.0
Diseases of the arteries, arterioles and capillaries	2 852	27.8	10.4
Diabetes mellitus	2 281	22.3	9.8

2023



Health statistical yearbook

Premature Cancer Mortality in Cuba

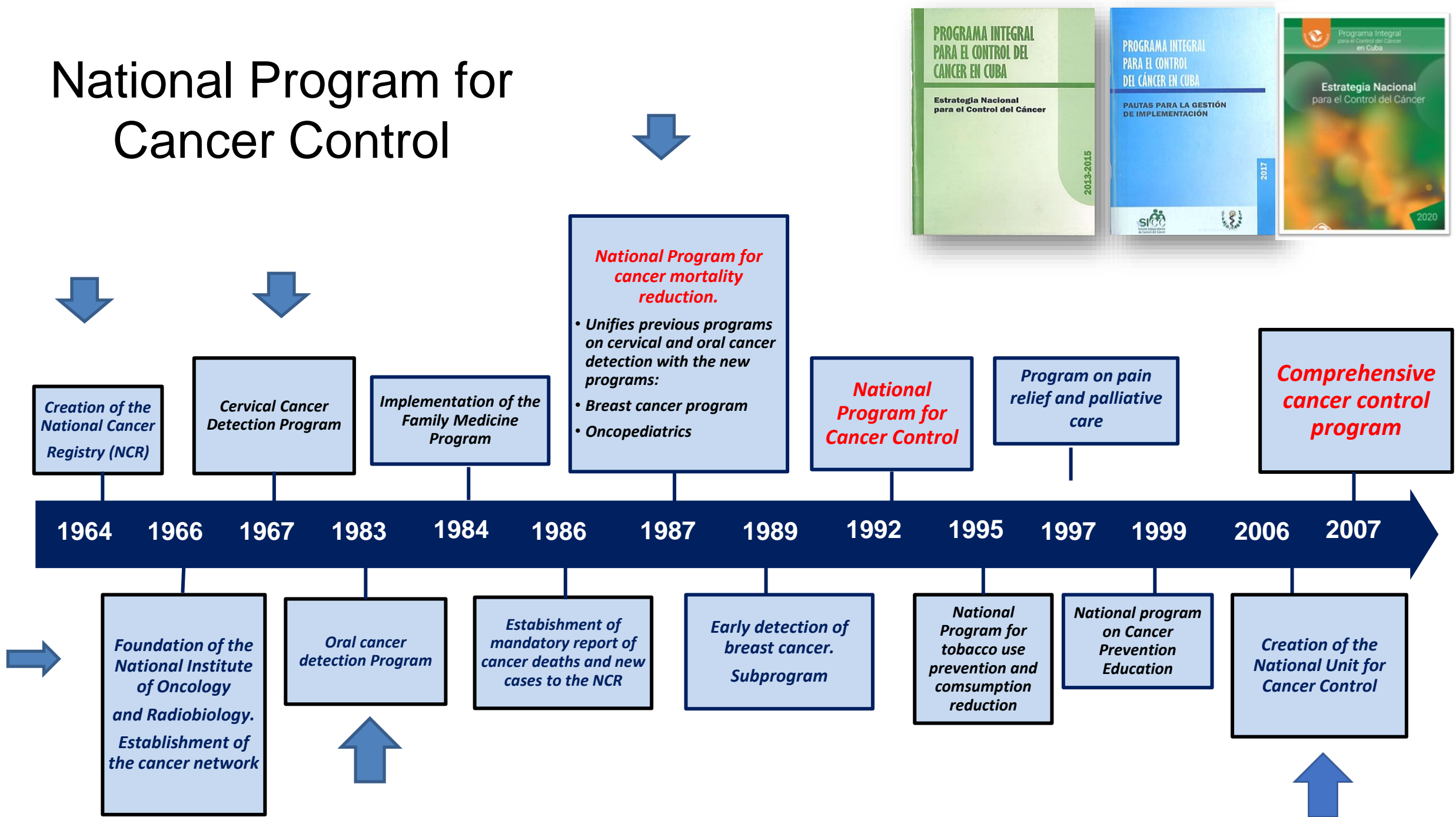
Premature mortality (30-69 years) according to selected causes and sex. Cuba 2022

	Male		Female		Total	
	No	Rate	No	Rate	No	Rate
Cardiovascular Diseases (I05-I52)	5 219	174.2	2 990	97.4	8 209	135.3
Malignant Tumors (C00-C97)	5 866	195.7	4 904	159.7	10 770	177.5
All causes	22 343	745.4	14 500	472.3	36 843	607.2

Cancer: First cause of premature death

1 in 3 deaths in Cuba between 30 and 69 years old is due to cancer

National Program for Cancer Control



Registro de Cáncer de Cuba: 1964-2024

*60 años al servicio de la vigilancia del
cáncer en Cuba*



<https://temas.sld.cu/estadisticassalud/>
<http://www.rnc.sld.cu/>

Among the oldest
population-based cancer
**registries in Latin America
and the Caribbean**

Currently, it is the **cancer
registry with the largest
population coverage** in the
Latin American and
Caribbean region.



**LOS REGISTROS DE CÁNCER DE BASE
POBLACIONAL SON UN ELEMENTO CLAVE
PARA EL CONTROL DEL CÁNCER**

Cuban Essential Cancer Drugs List

- Prevalence of different tumor types.
- Calculation of needs for oncological and support drugs according to the number of patients and clinical stages (National Cancer Registry).
- Classification of malignant tumors according to the degree of curability, prioritizing those drugs that benefit most patients.
- Compliance with WHO essential medicine list.
- Incentive for the national industry
- Introduction of high-quality generics and biosimilars.
- Dedicate import substitution resources to the **incorporation of new drugs.**
- Periodic update of treatment guidelines (evidence based medicine).



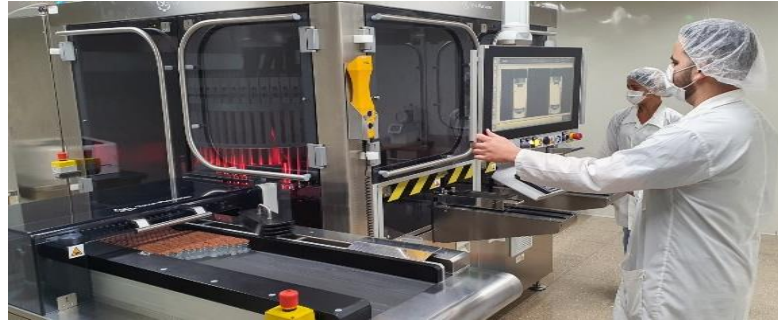
BIOCUBAFARMA



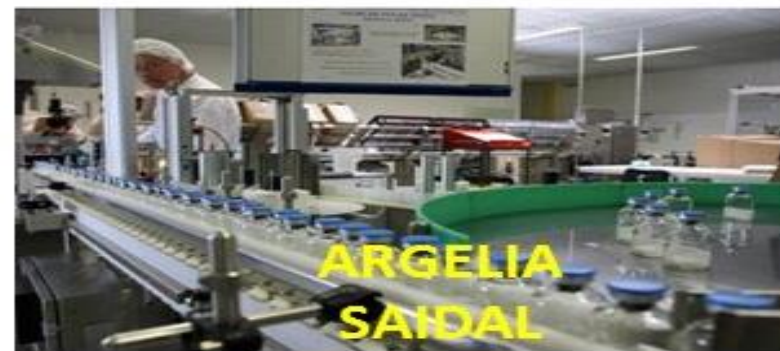
32 Enterprises
80 Manufacturing Facilities
+ 15 000 Workers



Production systems with high standards in compliance with Good Manufacturing Practices



Technology Transfer Cooperation





Center of Molecular Immunology: Leading biotech companies



Integrated with Ministry of Health

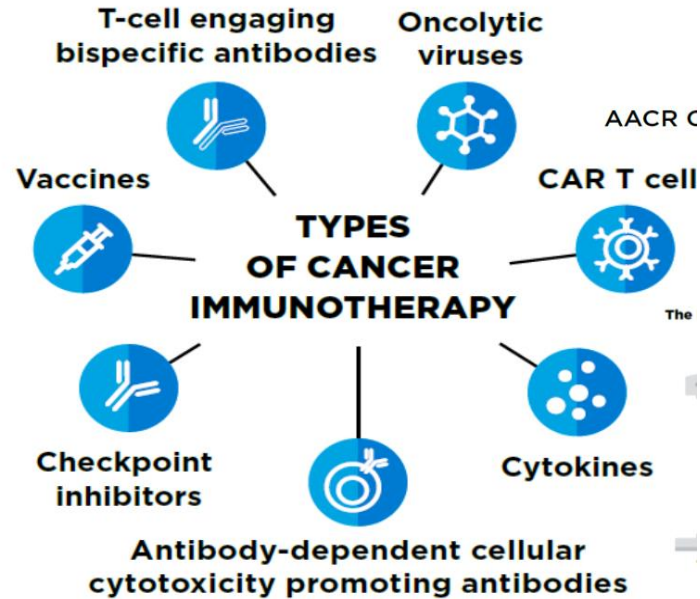


Mammalian Cell Fermentation



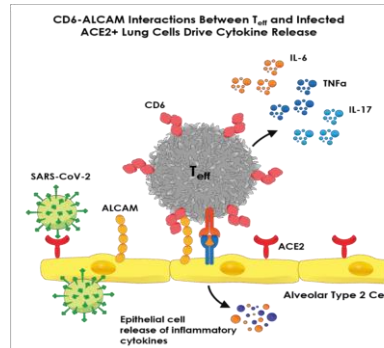
cencéc
CENTRO NACIONAL COORDINADOR DE ENSAYOS CLÍNICOS

Cancer Immunotherapy



> 1000 employees

Autoimmunity and inflammation



Neurodegenerative Disorders



Biosimilar Erythropoietin (ior® EPOCIM)

Treatment of anemia associated to:

- Chronic kidney diseases, in dialysis or pre-dialysis
- HIV
- Chemotherapy



3000, 5000, 30000, 40000IU(Pre-filled syringes)

Biosimilar Filgrastim (G-CSF)

Treatment of Neutropenia associated to:

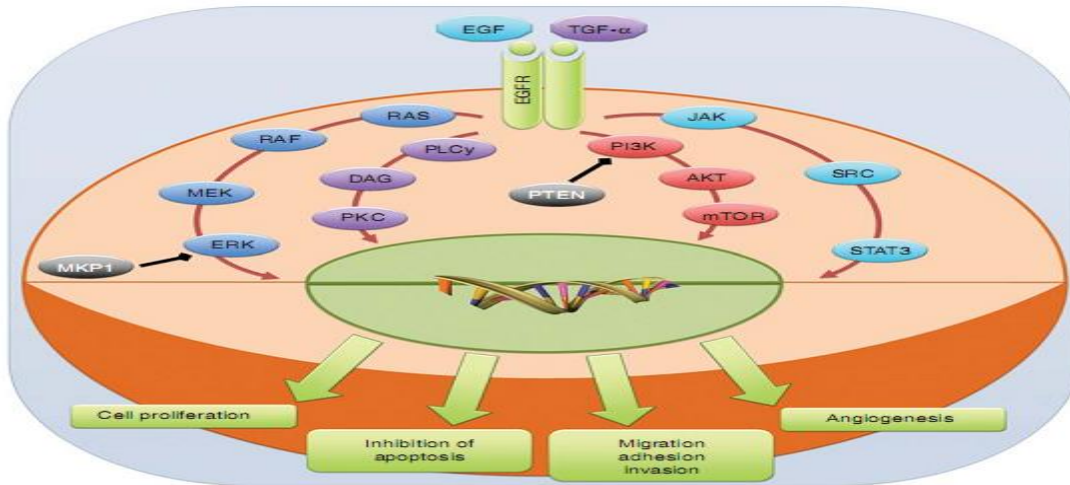
- Myelosuppressive chemotherapy in solid tumors, leukemia, lymphomas and Bone marrow transplant, AIDS.



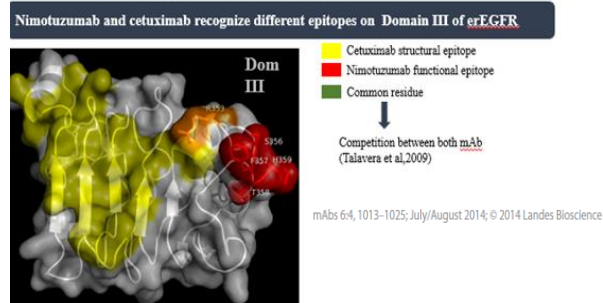
- Registered in Cuba in 2002

Two anti-PD1 biosimilars under development

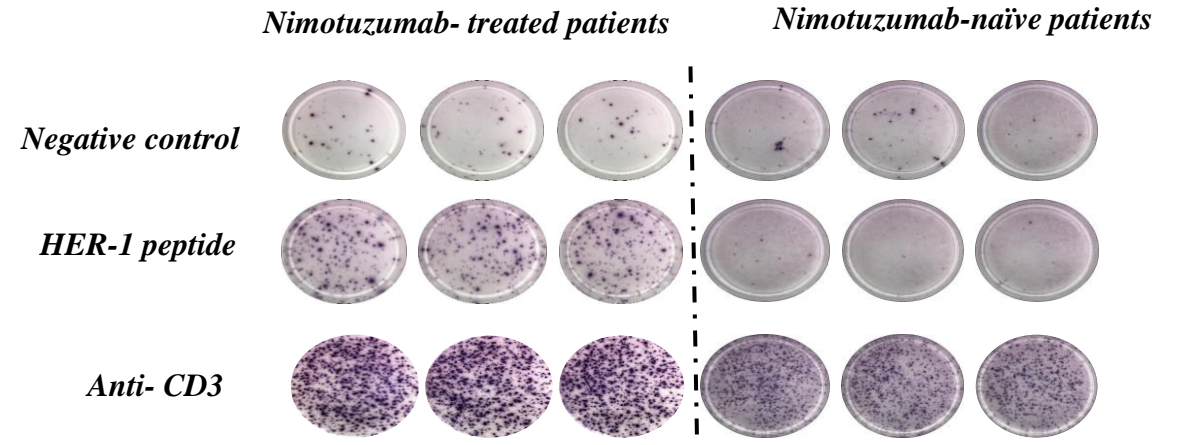
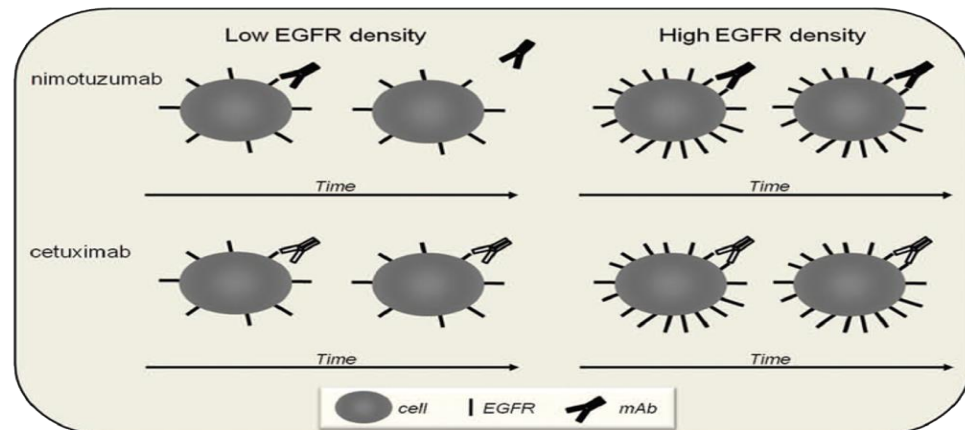
Nimotuzumab: Anti-EGFR MAb



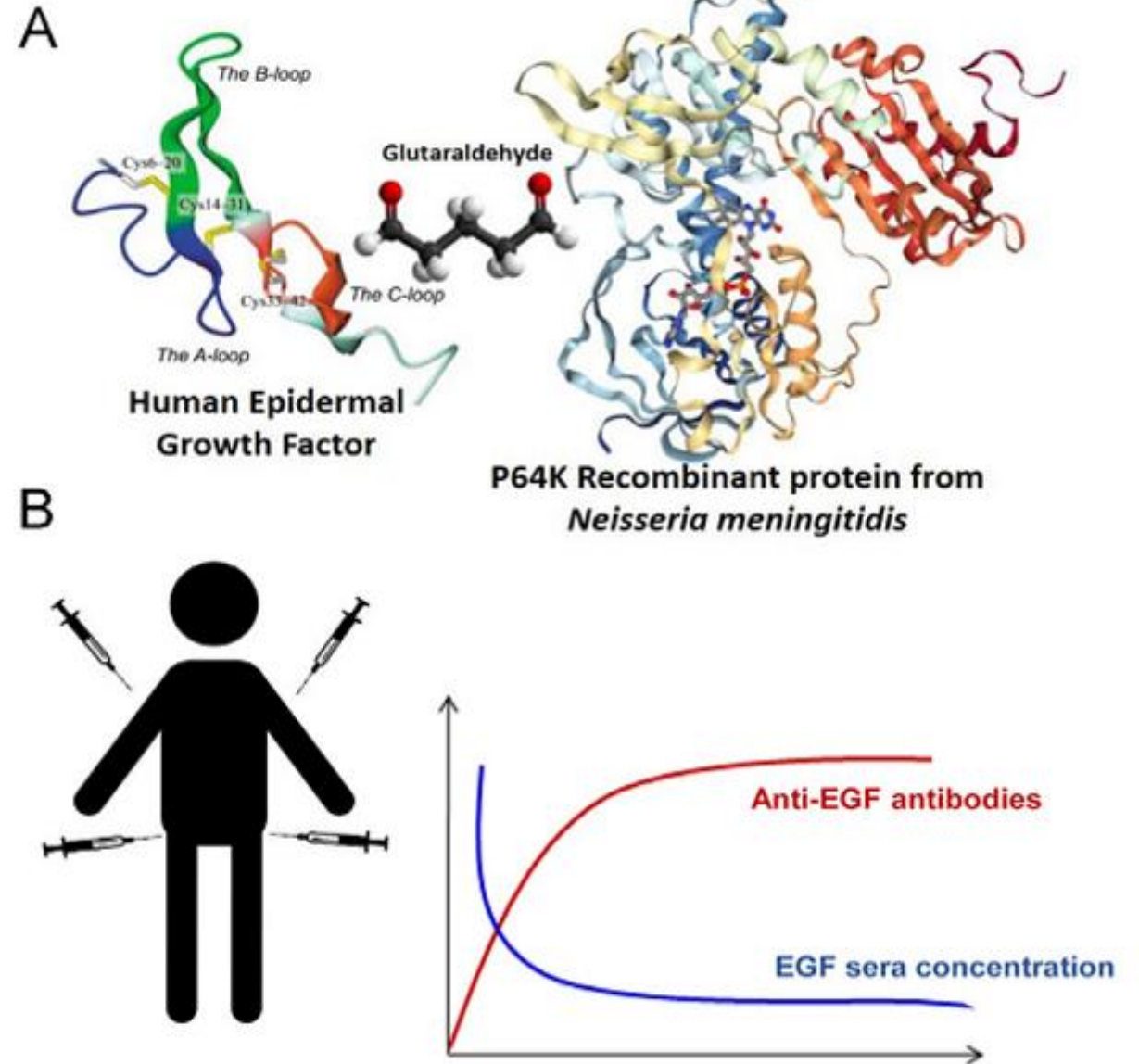
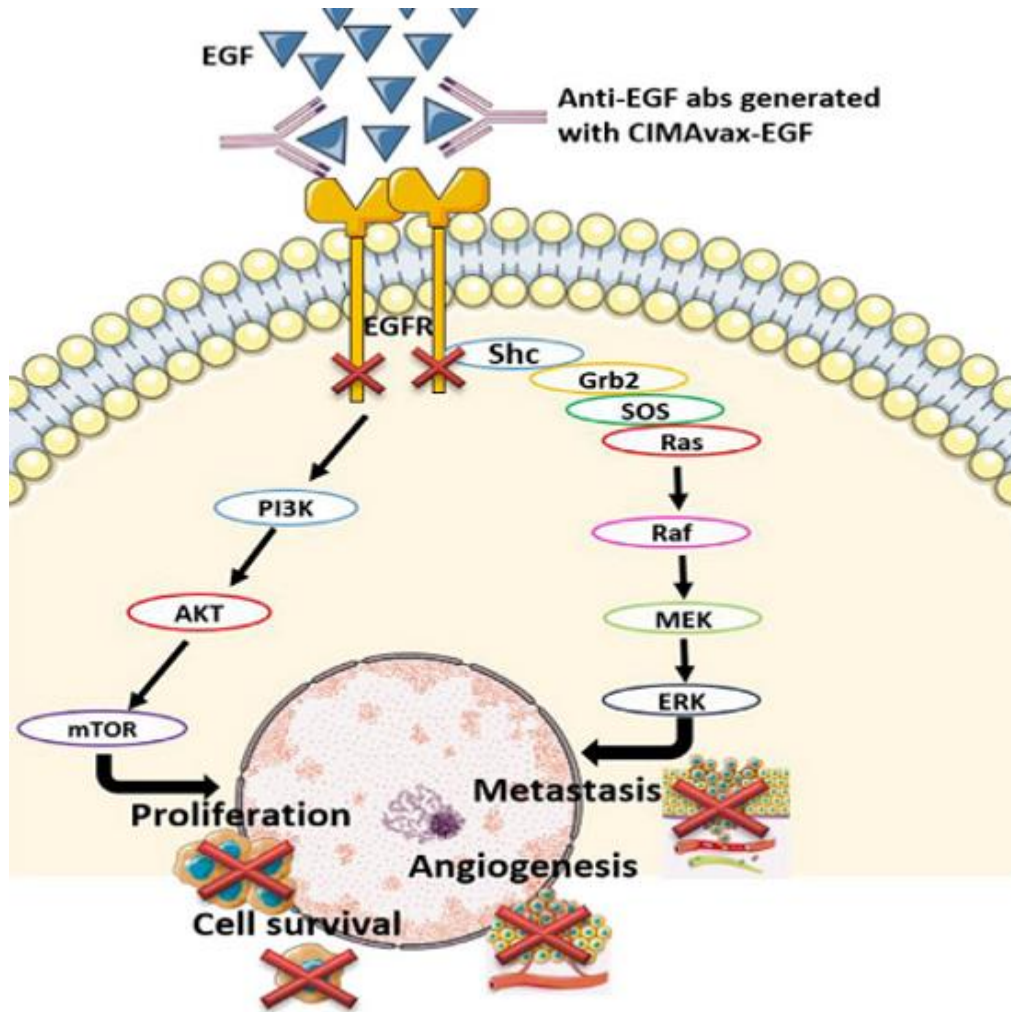
- **Humanized IgG1 MAb**
- **Intermediate affinity antibody against EGFR**
- **Low toxicity: No skin rash or hypomagnesemia.**
- **Treatment of pediatric patients**
- **Long term use possible.**
- **Approved for the treatment of SCCHN, NPC, glioma (children & adults), NSCLC, pancreatic ADC**
- **T cell response**



Nimotuzumab Induces NK Cell Activation, Cytotoxicity, Dendritic Cell Maturation and Expansion of EGFR-Specific T Cells in Head and Neck Cancer Patients



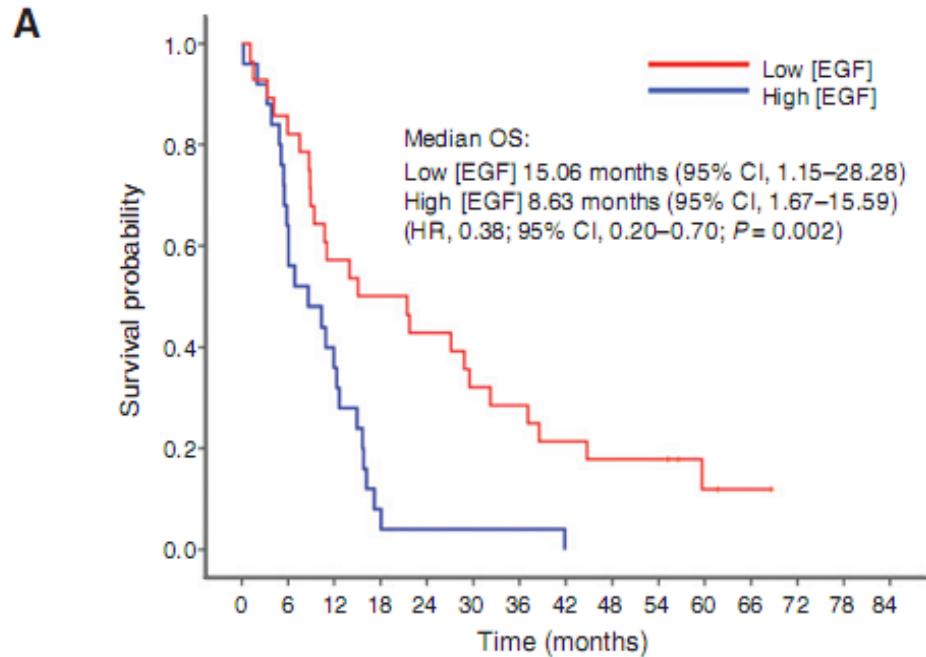
CIMAvax-EGF: EGF depleting immunotherapy



[EGF] was a worse prognostic biomarker for NSCLC & a good predictive biomarker for CIMAVax-EGF

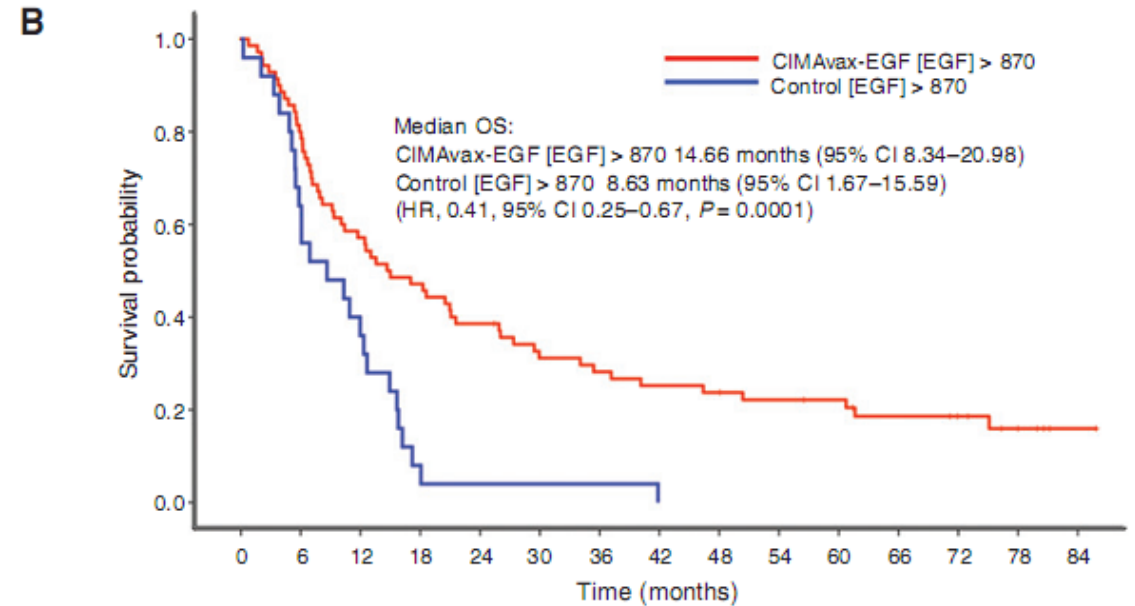


Control patients
Prognostic biomarker



Number at risk	0	6	12	24	36	48	60	72
Low [EGF]	25	23	16	12	8	5	2	0
High [EGF]	28	16	9	1	0	0	0	0

Vaccinated vs. controls with high [EGF]
Predictive biomarker



Number at risk	0	6	12	24	36	48	60	72	84
CIMAVax-EGF	70	56	40	27	19	16	12	8	1
Control	28	16	9	1	0	0	0	0	0

CIMavax-EGF administration in the primary care setting

2009-2015

- 45 Primary Care Units
- 24 Secondary Care Units
- 1084 patients!!
- Feasible!!
- Better access!!!
- Better treatment compliance!!



2016-2022

- 119 Primary Care Units
- 24 Secondary Care Units
- [EGF] evaluation in the municipality
- Correlation between [EGF] and overall survival.
- eCRFs



3 clinical trials ongoing at the RPCCC with Cimavax-EGF

RECRUITING

NCT06011772

EGF-Depleting Therapy CIMAvax-EGF in Combination With Standard Therapy for RAS- and BRAF Wild-Type Metastatic Colorectal Cancer

Conditions

Colo-rectal Cancer

Locations

Buffalo, New York, United States

RECRUITING

NCT04298606

A Vaccine (CIMAvax-EGF) for the Prevention of Lung Cancer Development or Recurrence

Conditions

Chronic Obstructive Pulmonary Disease Lung Non-Small Cell Carcinoma Pneumonia Stage IB Lung Cancer AJCC v8 [Show 4 more conditions](#)

Locations

Buffalo, New York, United States

RECRUITING

NCT02955290

CIMAvax Vaccine, Nivolumab, and Pembrolizumab in Treating Patients With Advanced Non-small Cell Lung Cancer or Squamous Head and Neck Cancer

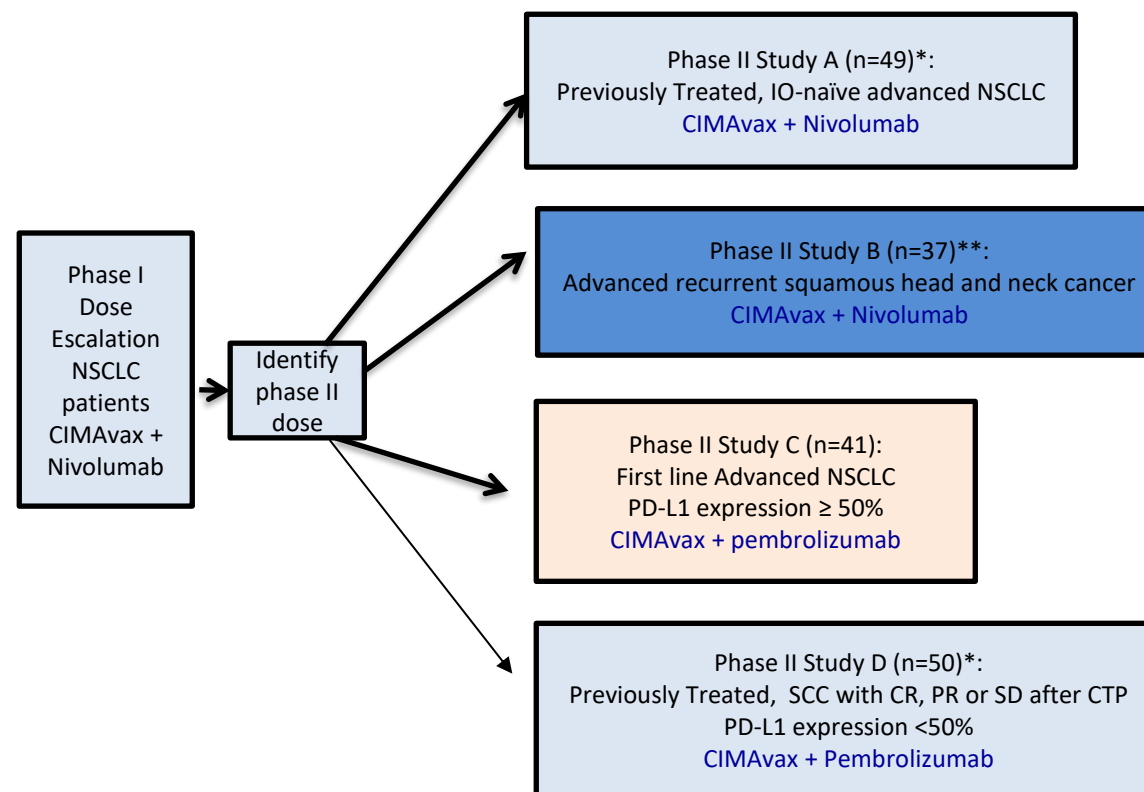
Conditions

Advanced Head and Neck Squamous Cell Carcinoma Advanced Squamous Non-Small Cell Lung Carcinoma Lung Non-Small Cell Carcinoma Metastatic Lung Non-Small Cell Carcinoma [Show 12 more conditions](#)

Locations

Indianapolis, Indiana, United States Buffalo, New York, United States Roslyn, New York, United States West Islip, New York, United States

A Phase I/II **Basket Trial** of the EGF Vaccine **CIMAvax in Combination with Anti-PD1** Therapy in Patients with **Advanced NSCLC** or Squamous Head and Neck Cancer



ClinicalTrials.gov



Augmenting antibody response to EGF-depleting immunotherapy: Findings from a phase I trial of CIMAvax-EGF in combination with nivolumab in advanced stage NSCLC

Rachel Evans¹, Kelvin Lee², Paul K. Wallace¹, Mary Reid¹, Jason Muhitch¹, Askia Dozier¹, Circe Mesa³, Patricia L. Luaces³, Orestes Santos-Morales³, Adrienne Groman¹, Carlos Cedeno¹, Aileen Cinquino¹, Daniel T. Fisher¹, Igor Puzanov¹, Mateusz Opyrchal², Christos Fountzilas¹, Tong Dai¹, Marc Ernstoff⁴, Kristopher Attwood¹, Alan Hutson¹, Candace Johnson¹, Zaima Mazorra³, Danay Saavedra³, Kalet Leon³, Agustin Lage³, Tania Crombet³ and Grace K. Dy^{1*}

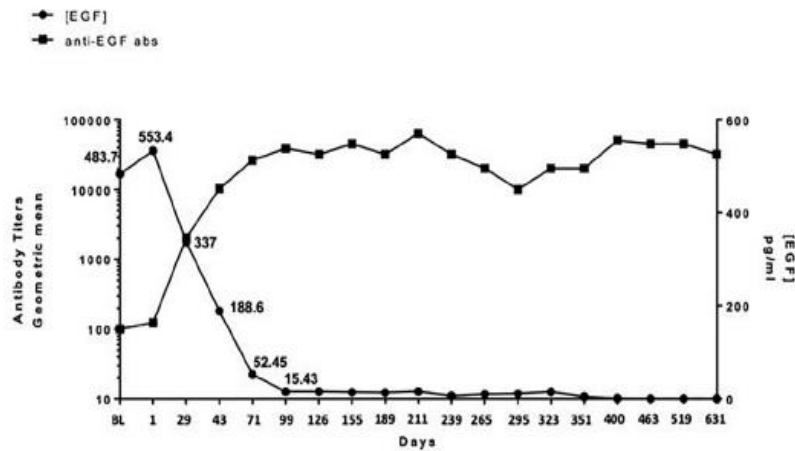


FIGURE 2 Relationship between anti-EGF antibody titers and serum EGF. There is a significant inverse correlation between circulating serum EGF and antibody titers in patients receiving CIMAvax-EGF in combination with nivolumab.

Faster immune response after Cimavax-EGF and nivolumab

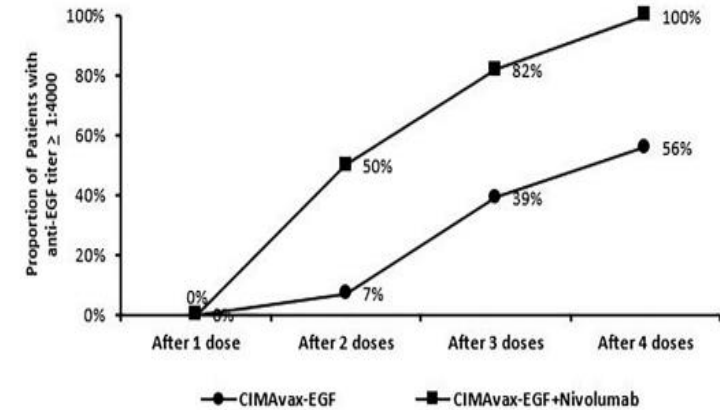
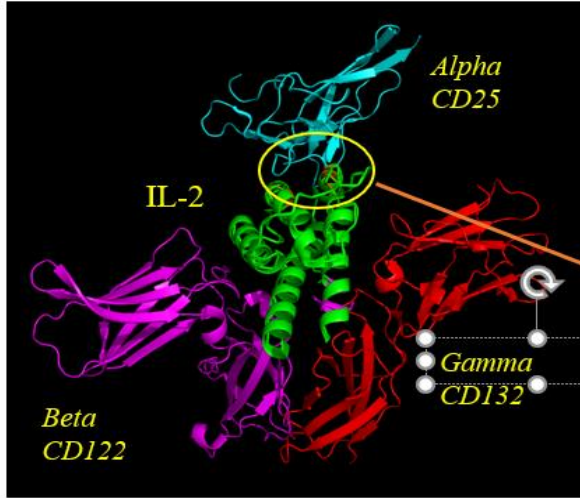
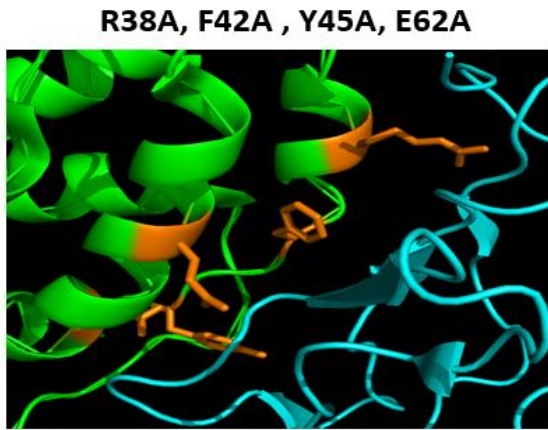


FIGURE 1 Trend of patients dosing and achieving anti-EGF titer $\geq 1:4,000$. Good anti-EGF antibody response ($\geq 1:4,000$) elicited at earlier time points in more patients receiving CIMAvax-EGF in combination with nivolumab compared to historical controls.

- **MOS= 18,3 months** (95 % CI: 6,8–NR) for patients completing vaccine induction
- **MOS= 21,7 months** (95 % CI: 1,8–NR) for KRAS wildtype patients.

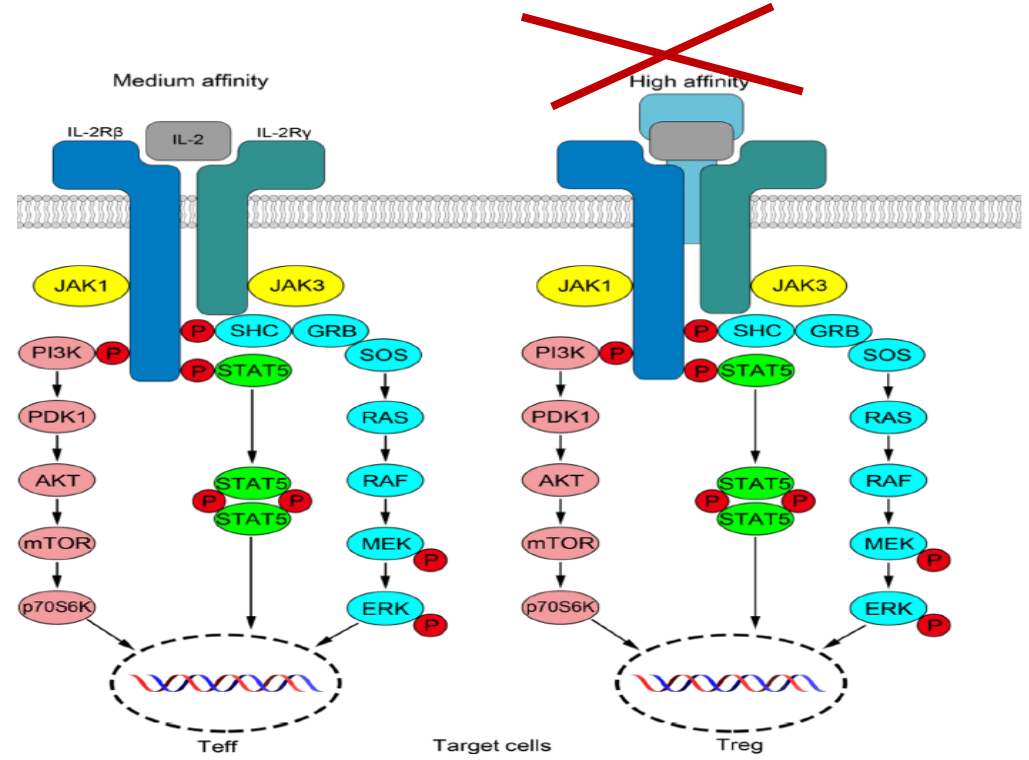


This IL-2 mutein will acts as an IL-2 agonist. It will activate the NK and memory CD8 T cells, but not the regulatory T cells



CD25 is overexpressed in Regulatory T cells
CD122 is slightly overexpressed in NK and memory T Cells

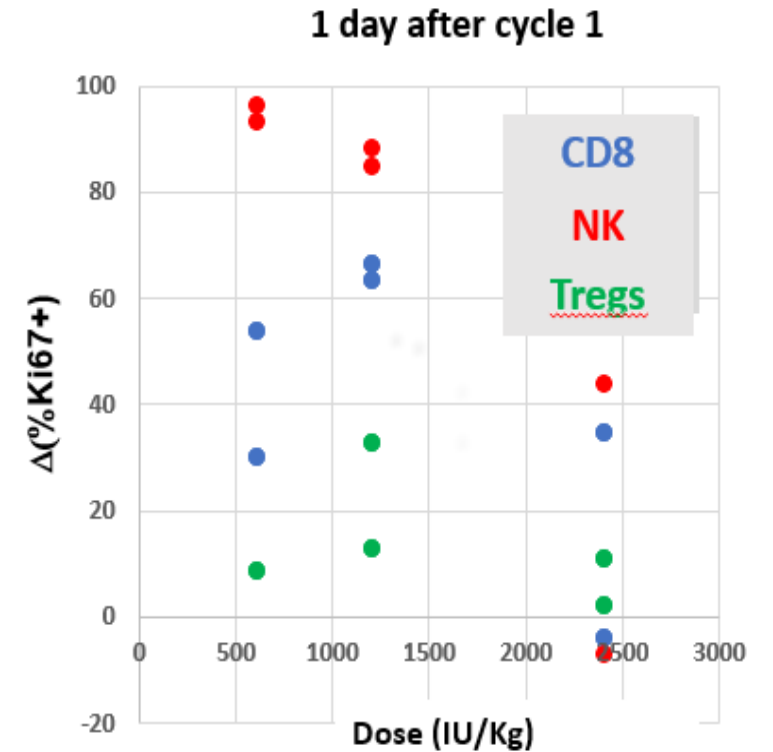
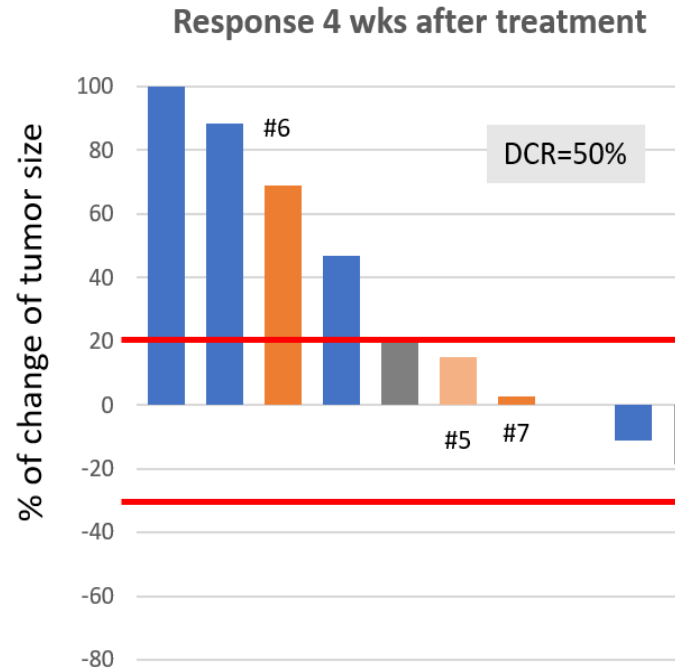
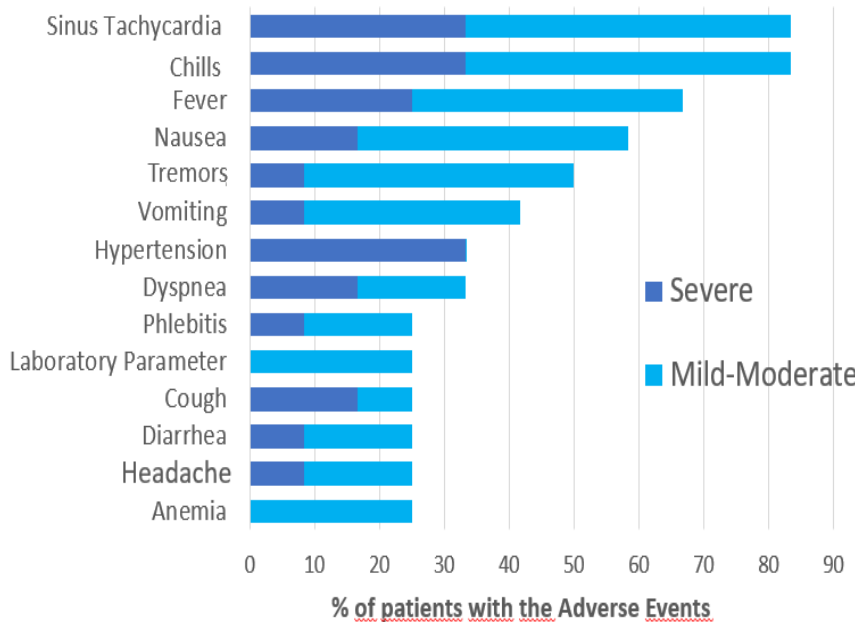
Carmenate T et al. J. of Immunology 2013; 190 (12), 6230-6238



IL-2 mutein

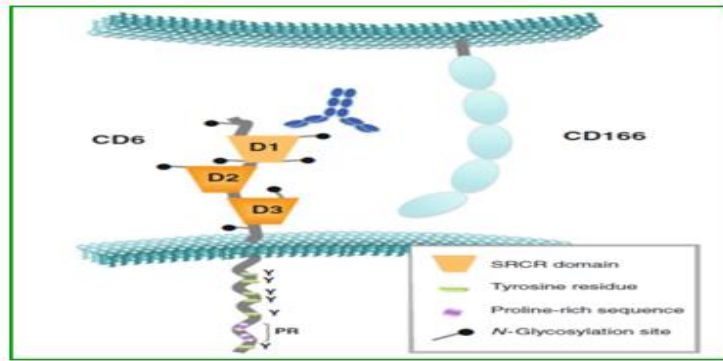
Preliminary safety and response data in very advanced cancer patients

Treatment-related adverse events reported in more than 3 patients (>20%), by intensity



No vascular leak or cytokine release syndromes

Itolizumab: Anti-CD6 Antibody

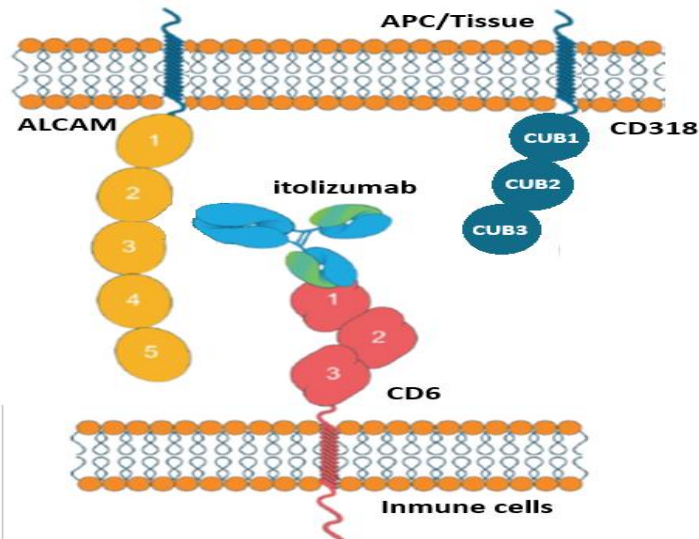


CD6 is a glycoprotein expressed on mature T-lymphocytes, NK and B1 cells
Crucial regulator of the T-cell activation

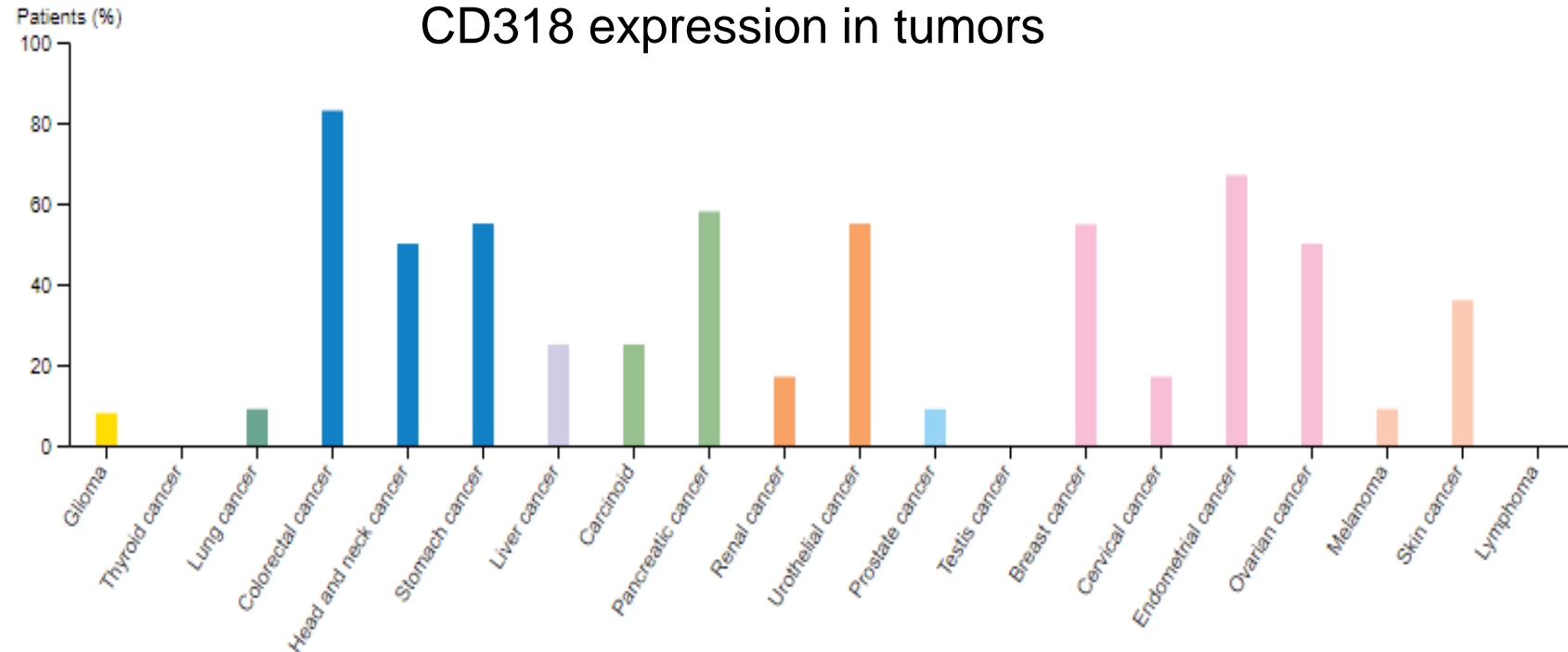


CD6-CD318

Tumoral immuno-evasive mechanism

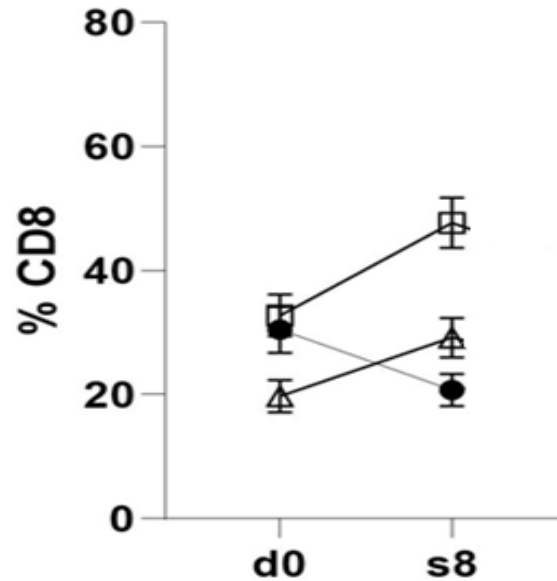


CD318 expression in tumors

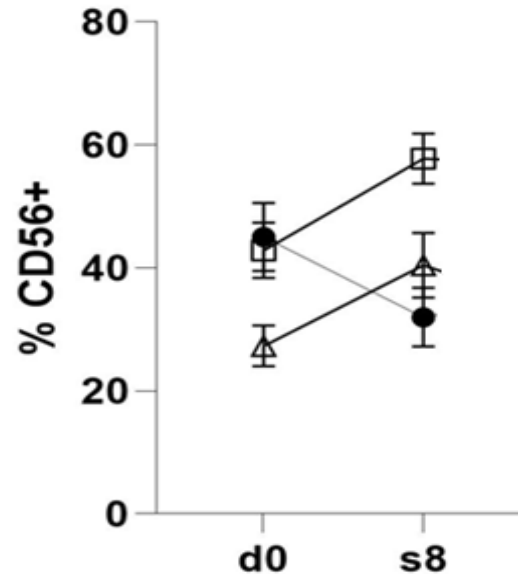


Itolizumab treated patients (advanced cancer)

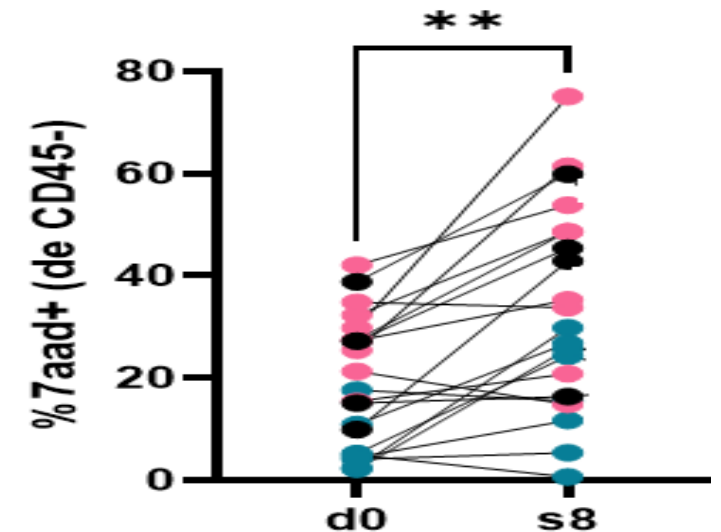
CD8+ T cells



NK cells



- NKG2A+
- NKG2D+
- △ Granzyme B+

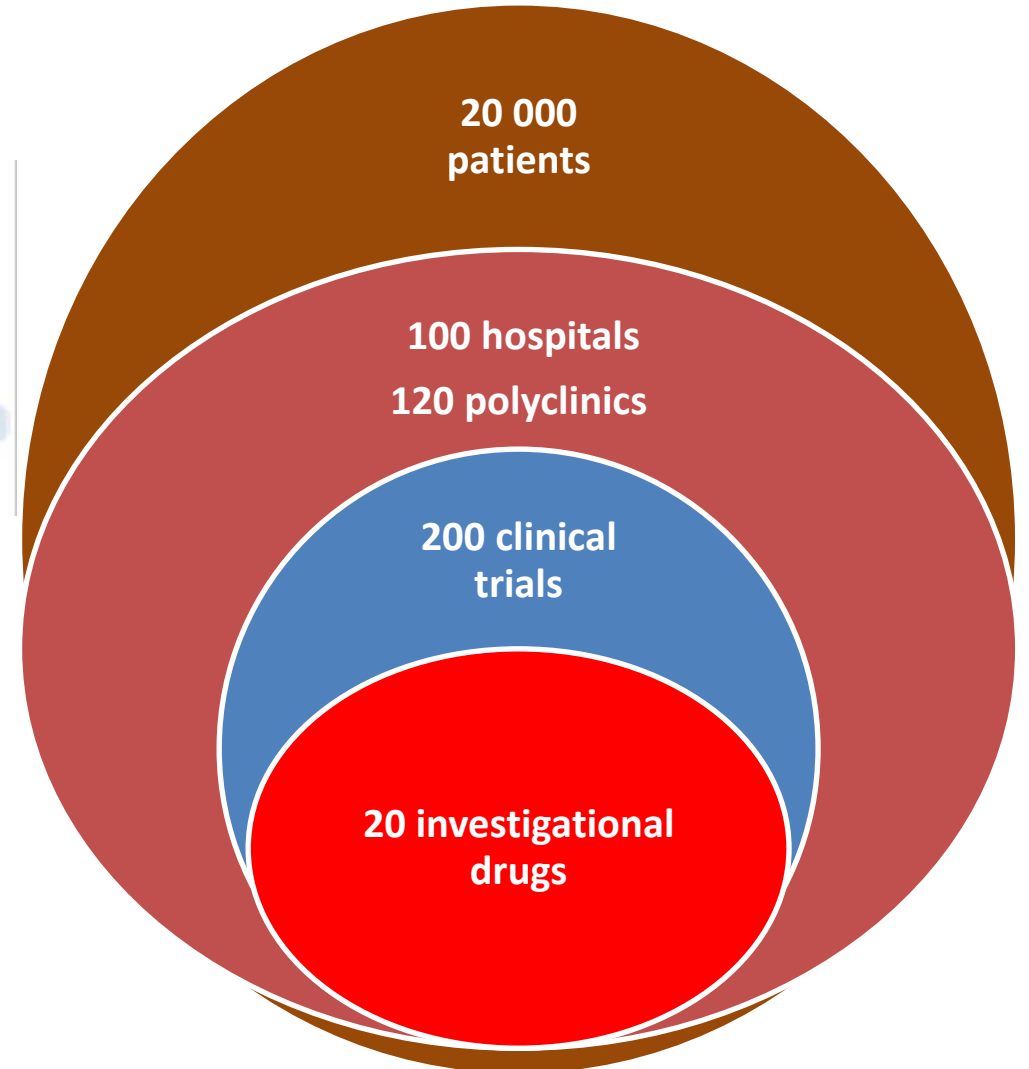


CD8+ T cells and NK cells

- Increase of NKG2D+ and granzyme B
- Decrease of NKG2A

Increased cytotoxic capacity of PBMC after 8 weeks of its treatment when co-cultured with CD318+ tumor cell lines (21 patients).

CIM: 30 years of clinical trials in Cuba



*SCIENCE IS OUR VOICE
TO CHANGE THE
FUTURE*

CENTRO
DE INMUNOLOGÍA
MOLECULAR



THANKS!!!