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Mexico

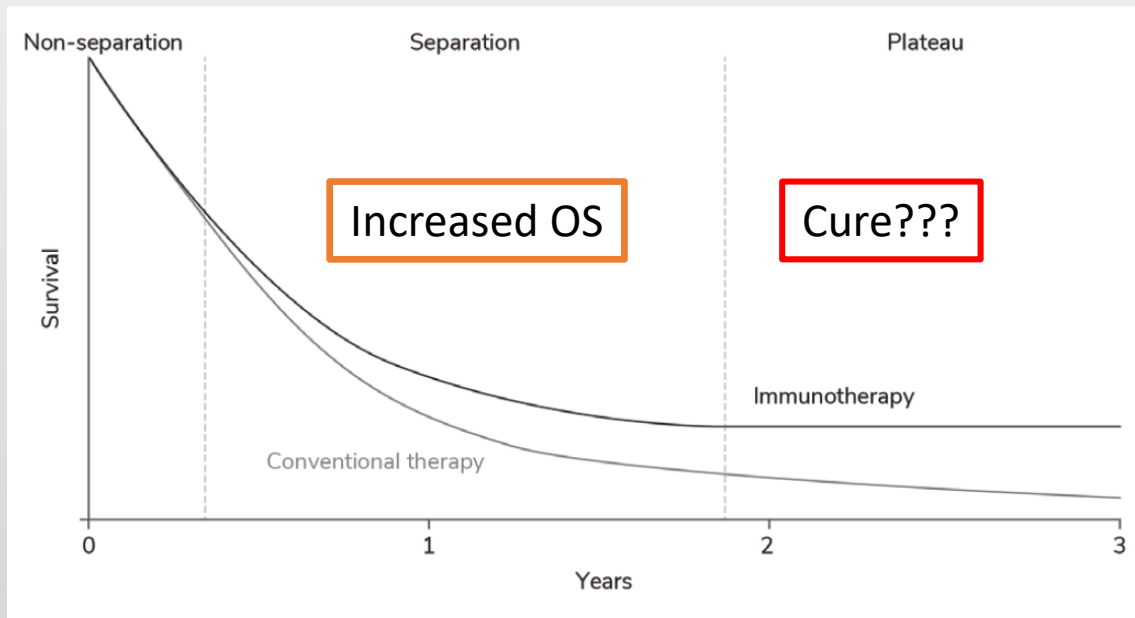
Access to immunotherapy in Mexico: Mission impossible?



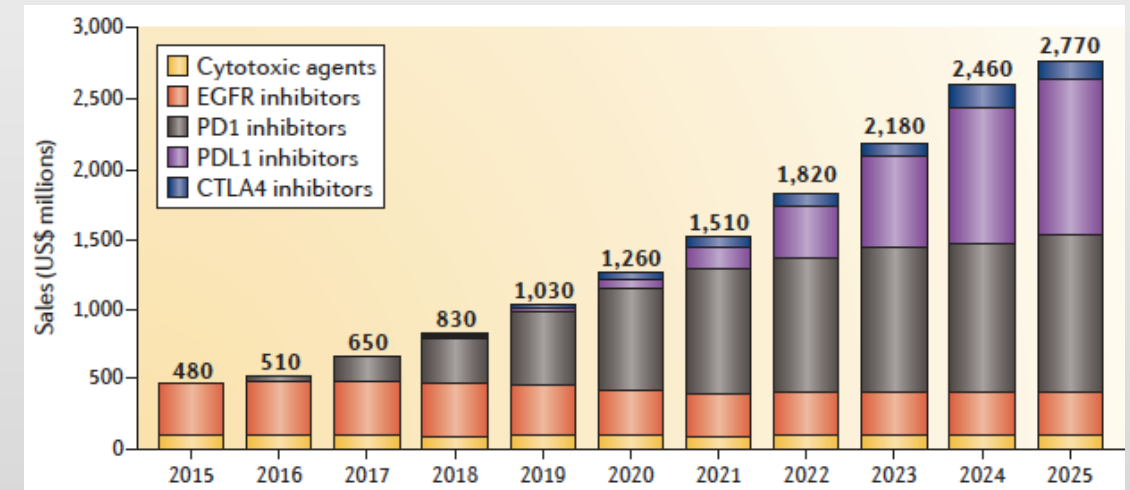
Disclosures

- Consulting fees: BMS, MSD, Merck, Janssen
- Contracted research: Pfizer, BMS, MSD

Immunotherapy has changed the cancer treatment paradigm



We all want to treat our cancer patients with IO!



IO treatments are expensive...

Mission: ~~im~~possible

AGENDA

- Facts about Mexico's health system
 - Cancer in Mexico
- Access to immunotherapy in Mexico
- Experience with immune-mediated adverse-events
- Areas of opportunity

Some facts about Mexico

- Population: 119,938,473 people.
- Mexico is the second largest economy in Latinamerica.
- According to the World Bank, Mexico is classified as an upper-middle-income country.



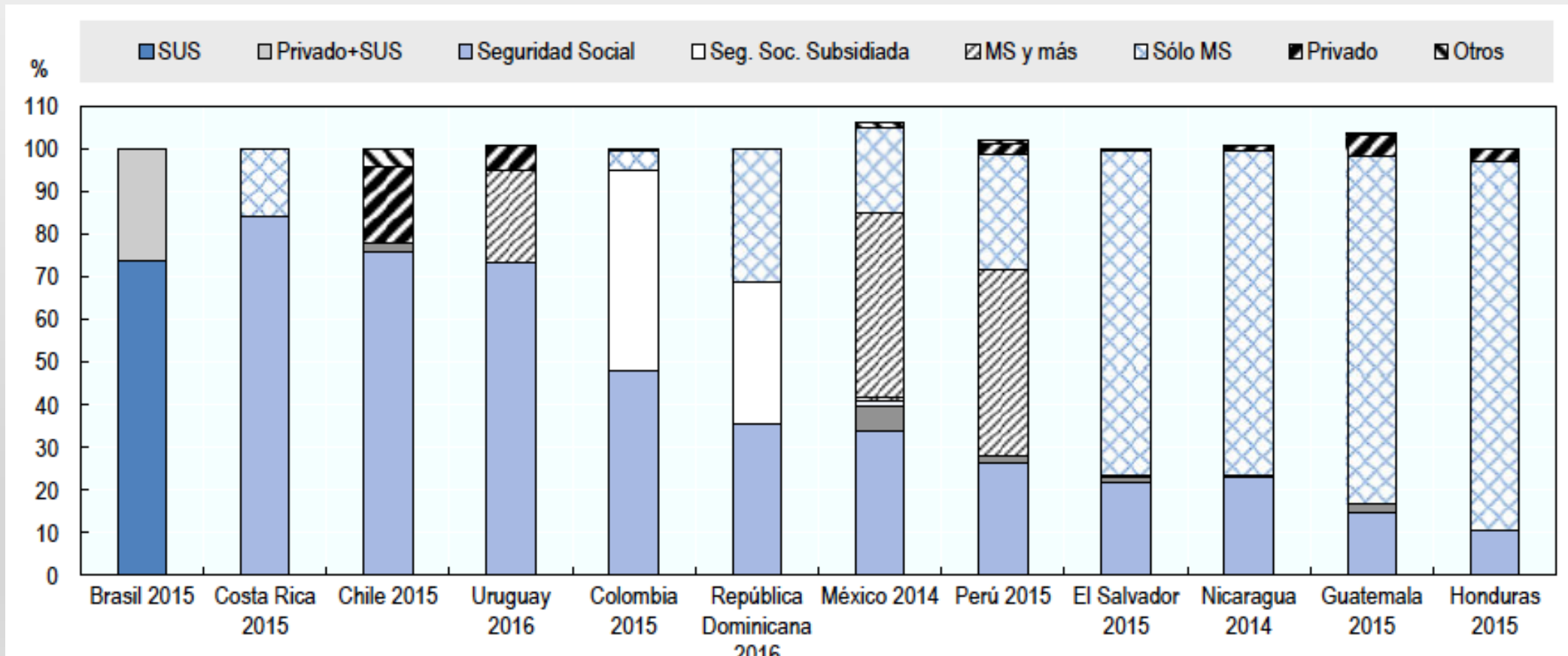
BUT...

- Mexico's economic growth has been 2% per year between 1980 and 2018.
- 41% of the population lives below the poverty-line determined for the country.



<https://data.worldbank.org/country/MX>

Health services fragmentation is frequent in Latinamerican countries.

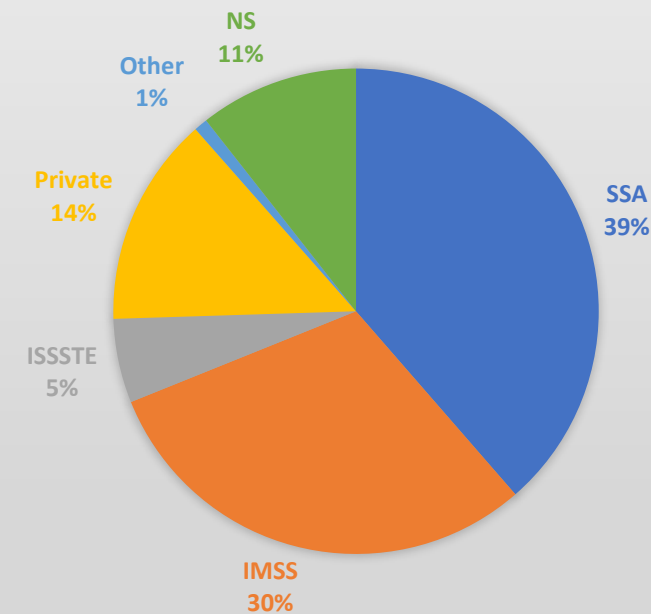


The health system in Mexico is complex

In 2016, 2.77% of the gross domestic product was spent in public health services.

- Health services are provided by different institutions:
 - IMSS. Formal workers.
 - ISSSTE. Government workers.
 - Secretaria de Salud (SSA). All other workers.
 - Other public health services. PEMEX, military assistance.
 - Private insurance.
 - 17% of people do not have any type of health coverage.

PROPORTION OF PATIENTS ATTENDED ACCORDING TO HEALTH INSTITUTION



NS. Non-specified.

Each public service has different guidelines and access to drugs.

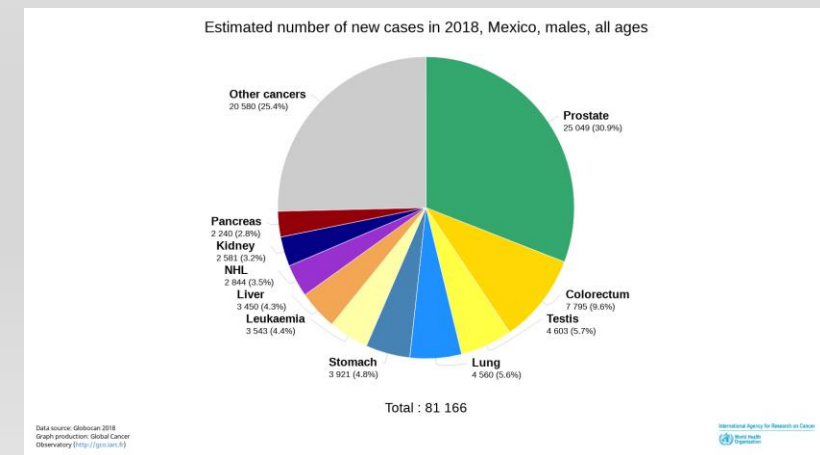
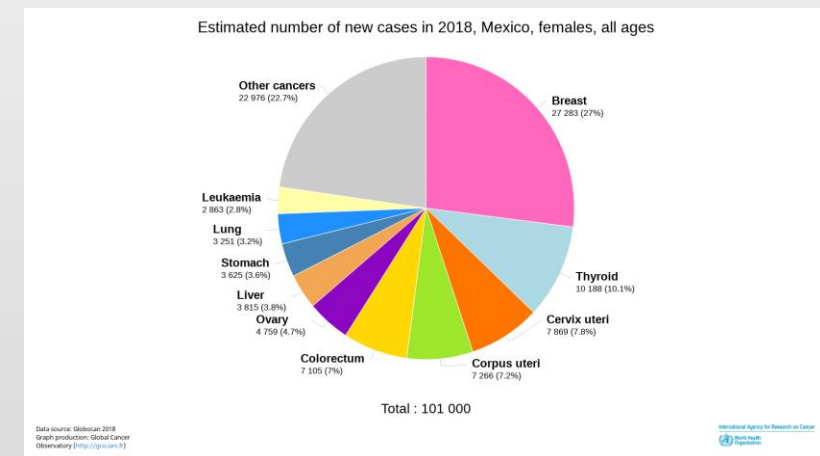
Cancer mortality and incidence in Mexico

Cancer is the 3rd most common cause of mortality in Mexico, causing 85,744 deaths in 2018.

It is estimated that there were approximately 190, 667 new cases of cancer in 2018 in Mexico.

Neoplasm	Number
Prostate	6,915
Lung	4,081
Colorectum	3,719
Liver	3,361
Stomach	3,201
Leukemia	2,449
Pancreas	2,106
Kidney	1,678
NHL	1,552
CNS	1,424

Neoplasm	Number
Breast	6,884
Cervix uteri	4,121
Liver	3,507
Colorectum	3,365
Stomach	2,833
Ovary	2,765
Lung	2,652
Pancreas	2,369
Leukemia	2,021
Gallbladder	1,302



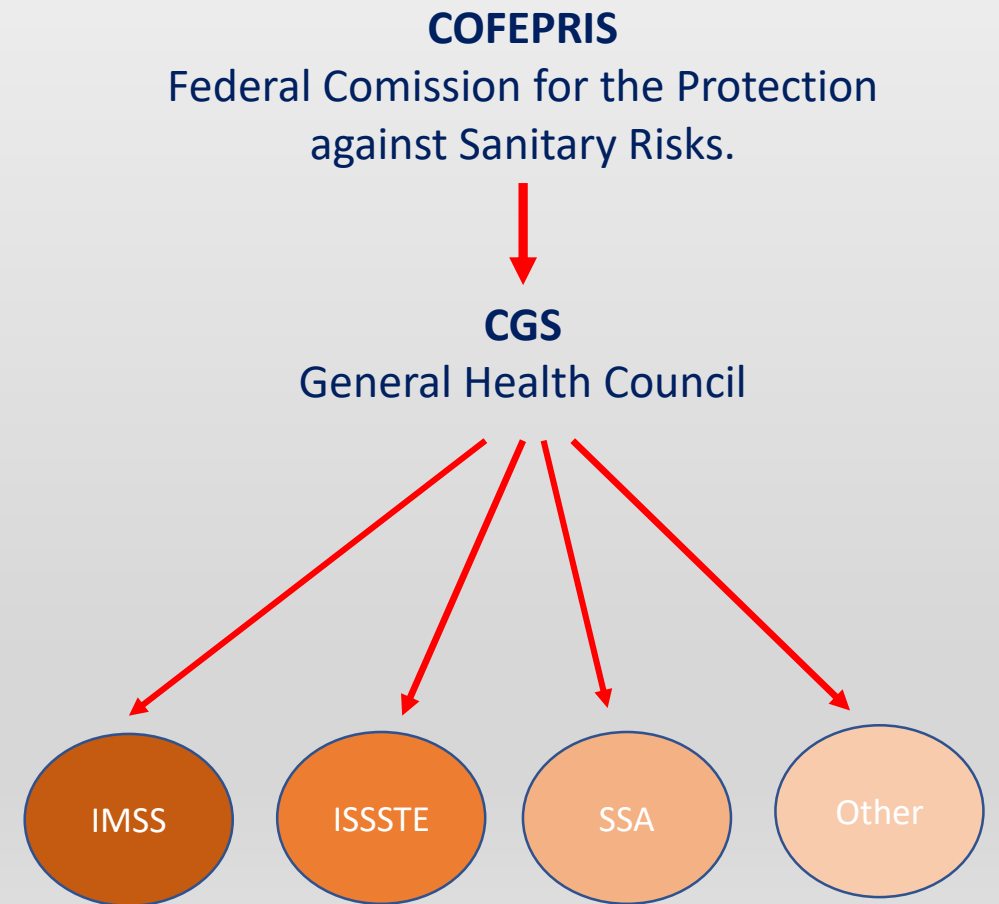
Infrastructure for treating cancer in Mexico

- **Approximately 70% of cases of cancer are diagnosed in advanced stages.**
- **Around 100 hospitals treat cancer in Mexico.**
- **2 specialized oncology hospitals (IMSS, SSA).**

There is a low oncologist/inhabitant ratio

Speciality	Number	Ratio / 100,000 inhab
Surgical Oncology	876	0.71
Gynecologic Oncology	151	0.29
Medical Oncology (adults and pediatric)	610	0.31
Radioncology	238	NA

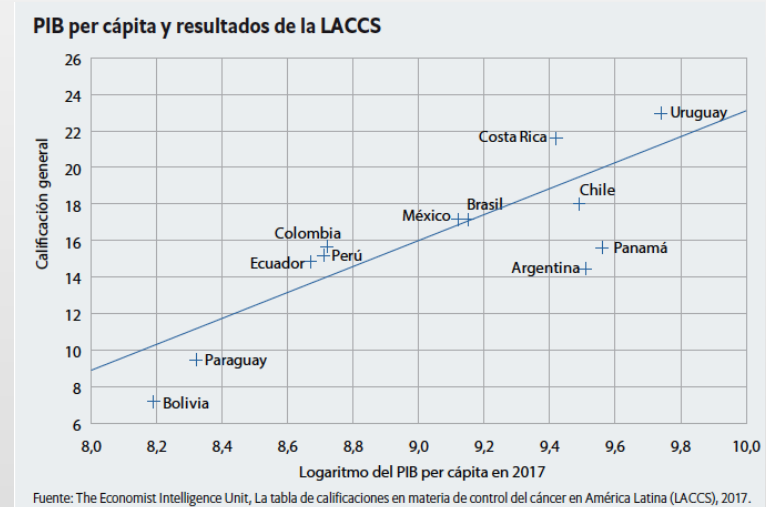
Drug Approval System is complex



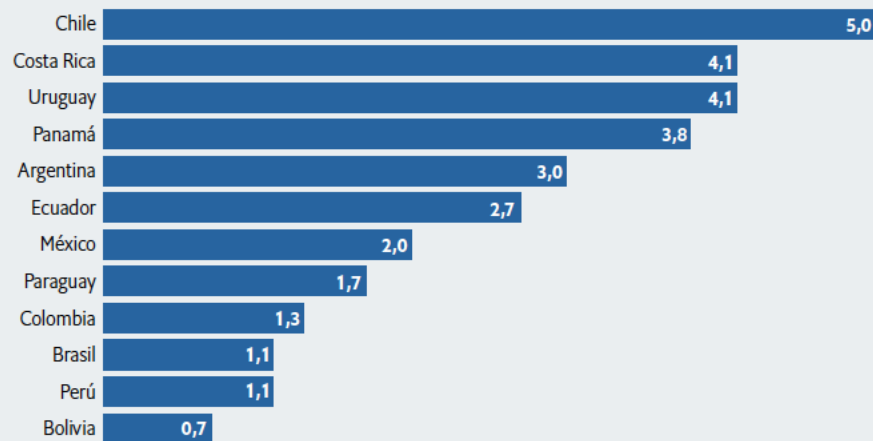
This type of infrastructure is similar across LatinAmerica.

Latinamerican Cancer Control score table

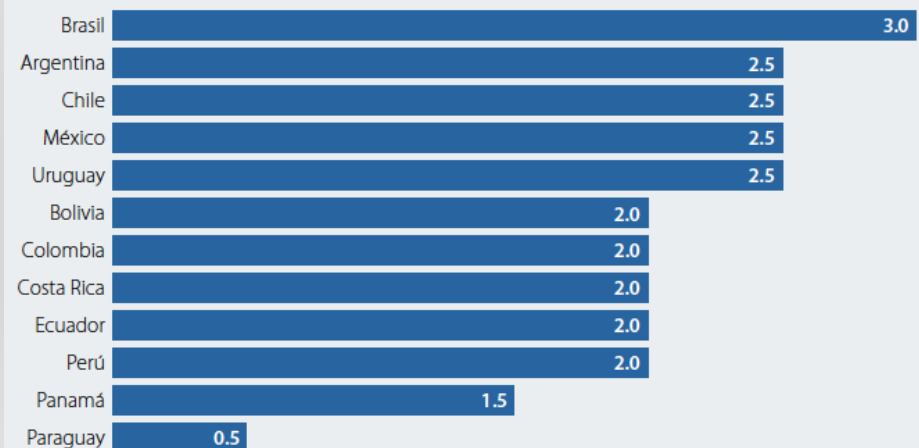
- Strategic plan.
- Performance supervision.
- Drug availability.
- Radiotherapy availability.
- Prevention and early detection
- Finance



Resultados de la LACCS en el campo «Disponibilidad de radioterapia», 2017



Resultados de la LACCS en el campo «Disponibilidad de medicamentos», 2017



Immunotherapy approvals in Mexico in 2019

	COFEPRIS	CSG	IMSS	ISSSTE	SSA
Atezolizumab	Metastatic lung cancer (2L)	Approved	No	No	No
Avelumab	Metastatic Merkel Cell Carcinoma	Not approved	--	--	--
Durvalumab	Lung cancer (after CT/RT)	Approved	No	No	No
Ipilimumab	Metastatic melanoma	Approved	No	Yes	No
	Metastatic CCRC	Not approved	--	--	--
Nivolumab	Metastatic melanoma	Approved	No	Yes	No
	Advanced melanoma (adjuvant)	Not approved	--	--	--
	Metastatic CCRC (2L)	Not approved	--	--	--
	Metastatic CCRC (1L)	Not approved	--	--	--
	Lung cancer (2L)	Approved	No	No	No
	Head & neck cancer (platinum refractory)	Approved	No	Yes	No
	Urothelial carcinoma (2L)	Not approved	--	--	--
	Hodgkin lymphoma	Approved	No	Yes	No
Pembrolizumab	Metastatic melanoma	Approved	No	No	No
	Metastatic lung cancer (1L)	Approved	Yes	Yes	No
	Metastatic lung cancer (2L)	Approved	No	No	No
	Urothelial carcinoma (2L)	Approved	No	Yes	No

In summary..

- Mexico is considered a middle-high income country.

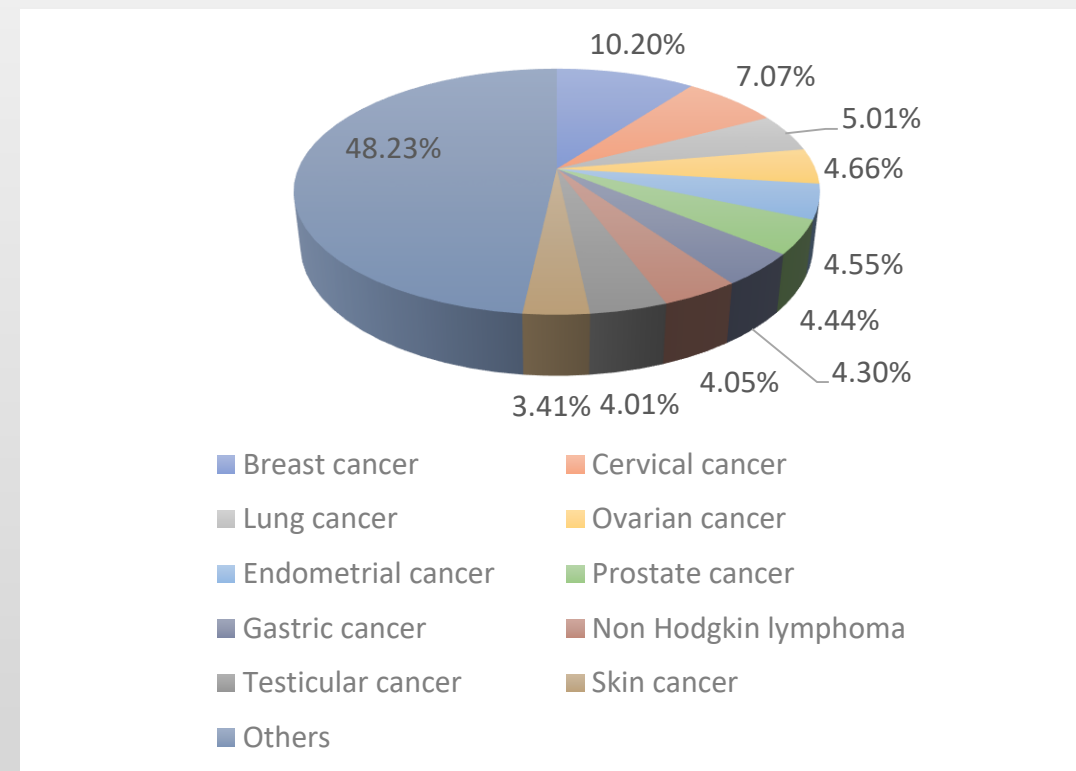
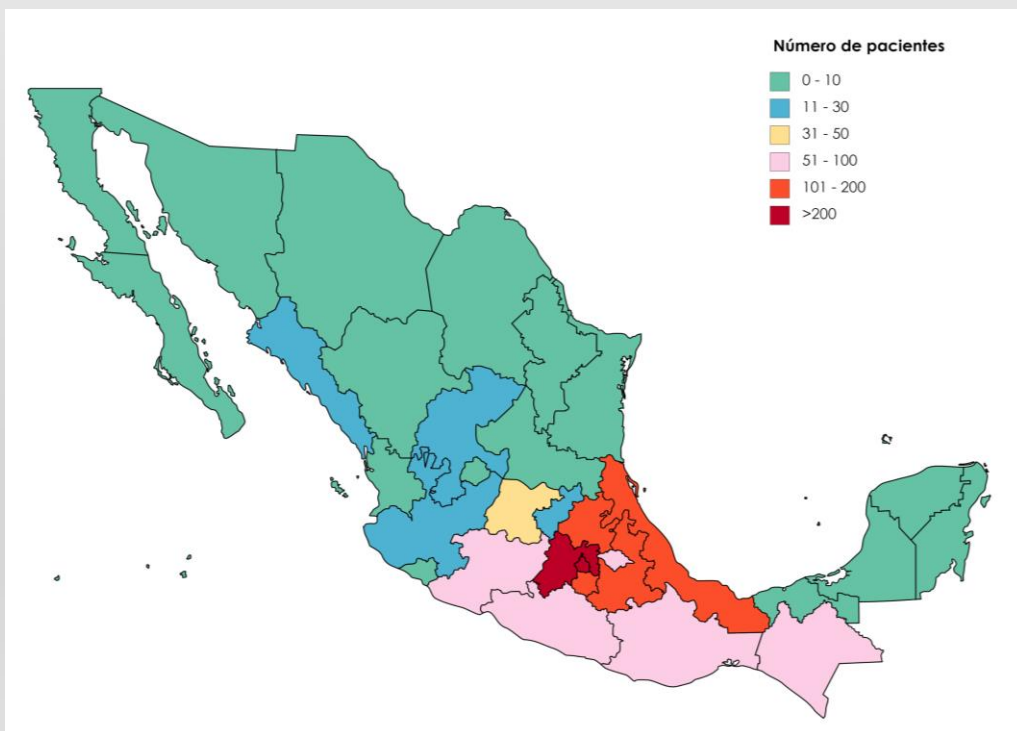
BUT..

- Cancer mortality still resembles a low-middle income country for some diseases.
- There are no objective data on cancer incidence in the country.
- Although a drug approval system is installed, and many immunotherapy approvals exist---

The problem is not approval,
the problem is access

National Cancer Institute, Mexico

- Academic hospital.
- National Health Institutes, SSA.
- In 2019, the institute provided 5,700 new consultations



How does our institution get access to systemic treatments?

INSABI (Former Popular Insurance)

National Program.
Government supported.
Covers diagnostic workup and treatment.

- Breast Cancer
- Testicular Cancer
- Prostate Cancer
- Colorectal Cancer
- Cervical Cancer
- Ovarian Cancer
- Lymphoma

Special Access Programs

Institutional program.
Government supported.
Funding for uncovered needs (usually treatment).

- Lung Cancer
- Ovarian Cancer
- Cervix Uteri Cancer

Clinical trials Expanded access trials

Public or private funding.

- Indistinct of pathology.
- Depends on availability.

Mixed tumors clinic

- Genitourinary tumors
- Head and neck cancer
- Skin cancer

INSABI

50% of our patients' therapies would rely on patient's income

Primary site	Patients (N= 188)	Curative intent treatment (N=77)	Palliative intent treatment (N=111)
Prostate	55	--	55
Testicular	36	35	1
SCHNC	33	28	5
Kidney	28	1	27
Melanoma	17	11	6
Urothelial	6	1	5
Thyroid	5	--	5
Penile	5	--	5
Skin, NM	3	1	2

At least 4 tumor types that could potentially be covered partially by immunotherapy clinical trials

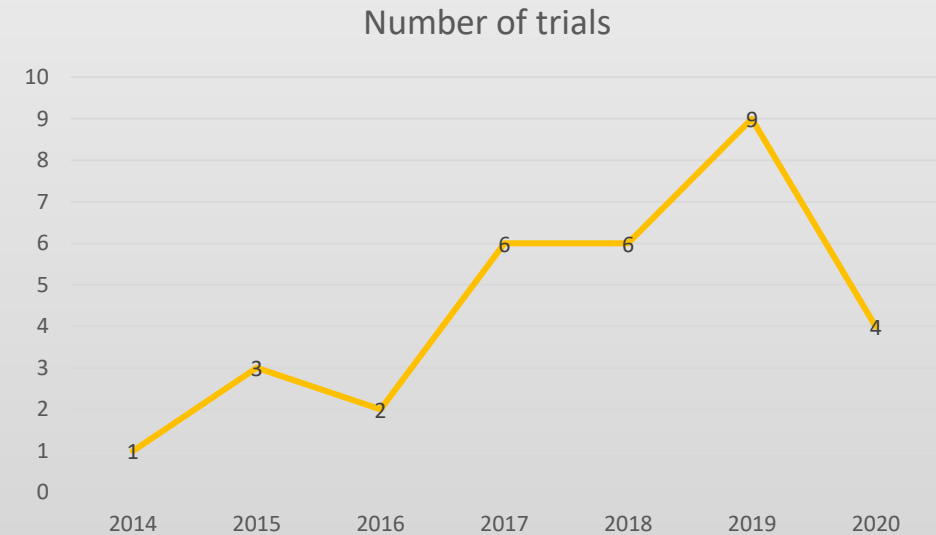
Mixed tumor clinic

- The clinic has had 15 industry-sponsored clinical trials or expanded access programs since 2011.
- 11 of these trials included an immunotherapy treatment.

Year	Indication	Type of program	Number of patients	Status
2014	Metastatic Melanoma	Clinical trial	1	Closed
2016	Metastatic CRCC	EAP	9	Closed
2017	Metastatic SCHNC	Clinical trial	19	FU
2017	Metastatic SCHNC	Clinical trial	11	Closed
2017	Metastatic Melanoma	Clinical trial	1	Closed
2018	Metastatic CRCC	Clinical trial	13	FU
2018	Metastatic Urothelial	Clinical trial	2	FU
2019	Metastatic Urothelial	Clinical trial	3	Recruiting
2019	Adjuvant CRCC	Clinical trial	2	Recruiting
2019	Metastatic CRCC	Clinical trial	17	FU
2019	Adjuvant Melanoma	Clinical trial	3	FU

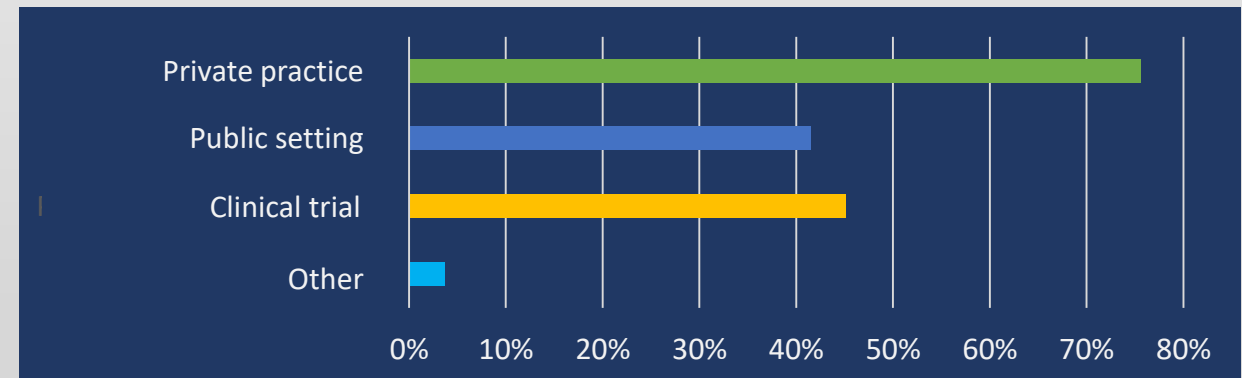
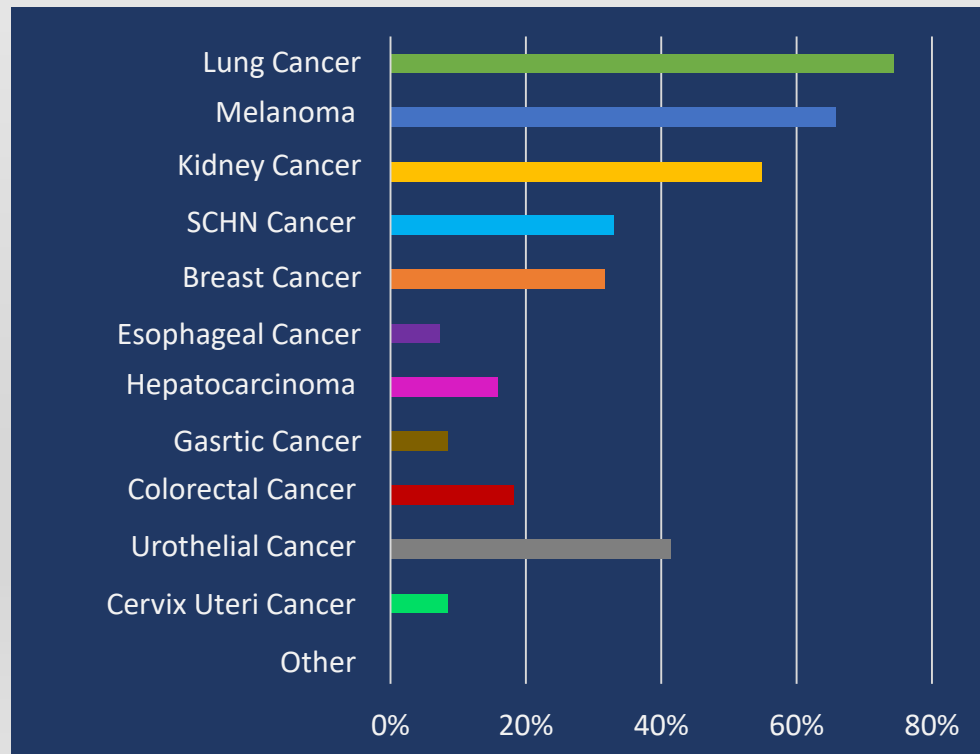
Multiple tumors can fit immunotherapy clinical trials

Indication	Number of trials	Number of patients treated
Lung cancer	10	136
Hepatocarcinoma	3	10
Esophageal/Gastric	4	11
Ovarian	1	4
Cervical	2	27
Breast	4	NA



Experience with immunotherapy in Mexico

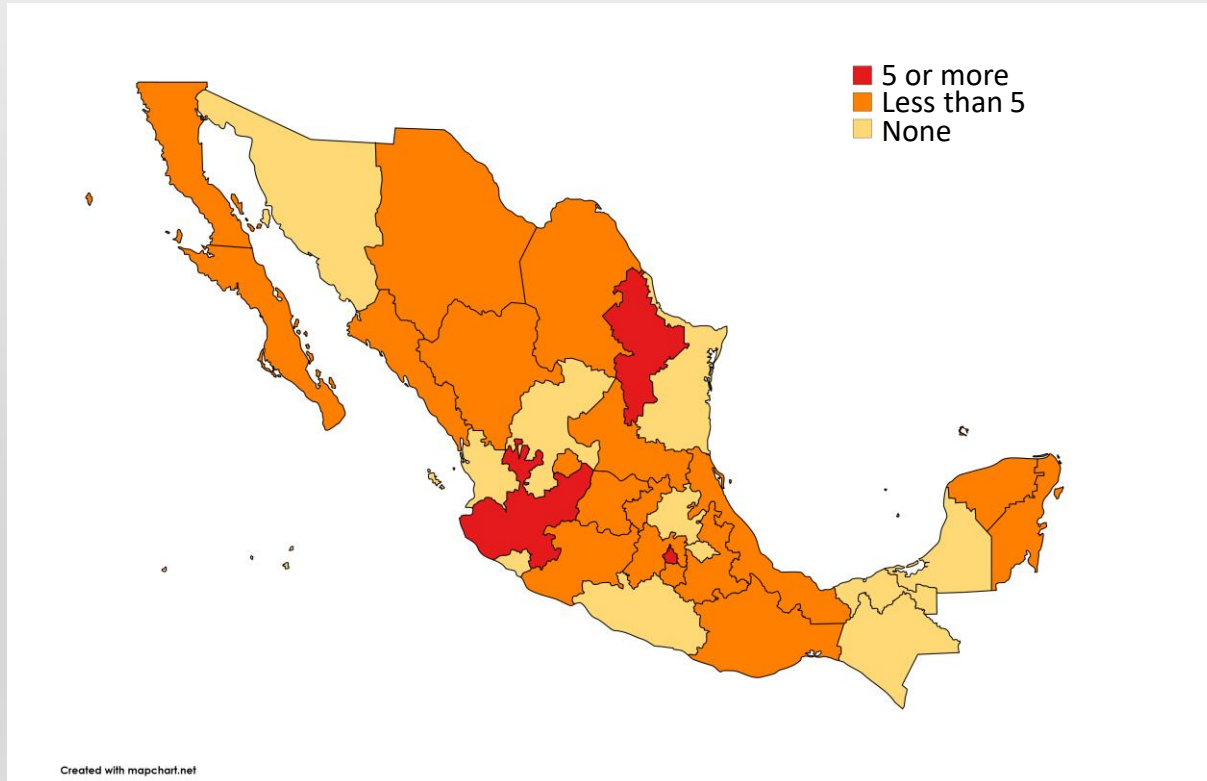
- National Survey on immunotherapy access 2020.
- 89 medical oncologists responded.
- 92% have had experience with immunotherapy.



Access to clinical trials can be find all over the country

Networking is key!

States with Oncologic Clinical Trial Centres



Group administrator: Joaquin Reynoso, M.D.

Other ways of increasing access: Strategies to decrease costs

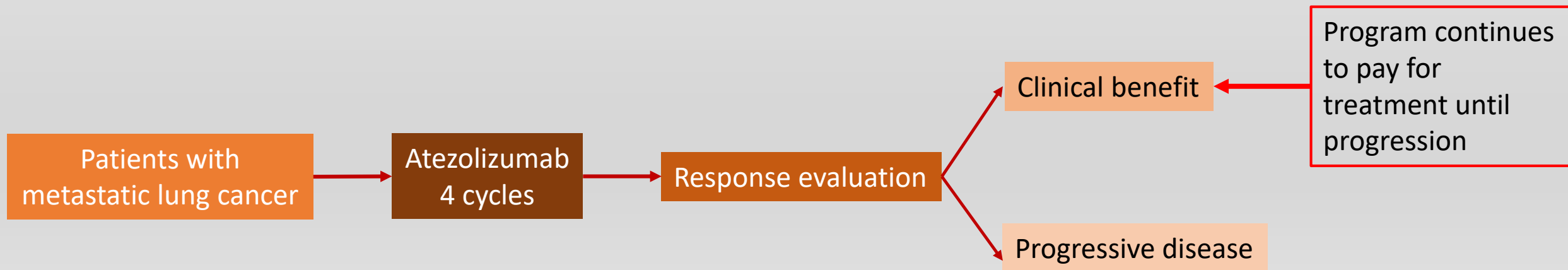
- Thoracic cancer Special Access Program.

Treatments covered by the program (metastatic lung cancer):

- First and second-line chemotherapy (only women).
- ALK-TKI
- EGFR-TKI
- Bevacizumab

Shared-risk programs

- Alectinib
- Atezolizumab



Other ways of increasing access: Strategies to decrease costs

- Fixed dosing vs weight-based dosing.

Initial dosing for nivolumab and pembrolizumab were based on weight.
Currently, fixed dosing for both drugs are approved worldwide.

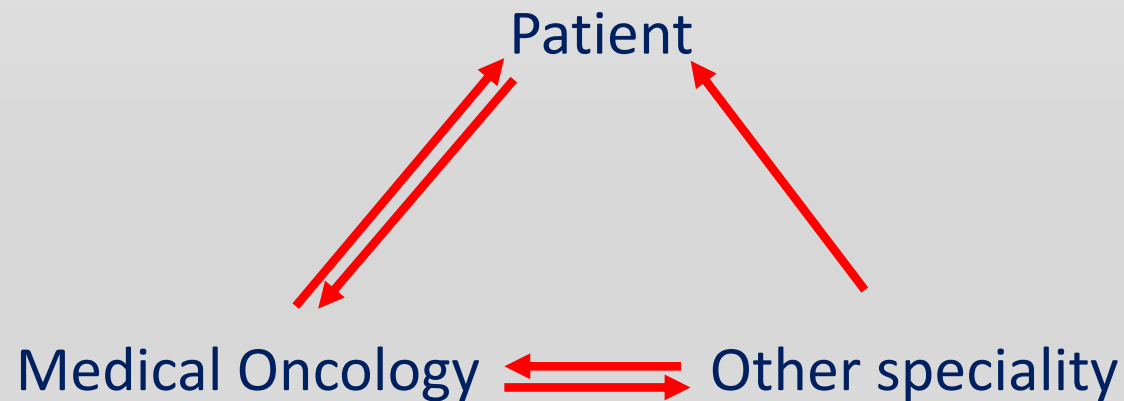
- 792 patients with metastatic lung cancer were analyzed.
- Median weight was 65kg (35-131)

PEMBROLIZUMAB (2 mg/Kg) Q3W vs 200mg Q3W						
Comparison	Total dose per cycle	Cost per cycle	Excess cost per cycle	Dose difference	Annual cost treatment (17 cycles)	Net difference annual cost per patient
Weight based dose (Median 65Kg)	130 mg	\$5171.4	\$2,782.6	70mg	\$87,913	\$47,305
Fixed-dose	200mg	\$7,954	NA	NA	\$135,218	NA
NIVOLUMAB (3mg/Kg) Q2W vs 240mg Q2W						
Comparison	Total dose per cycle	Cost per cycle	Excess cost per cycle	Dose difference	Annual cost treatment (26 cycles)	
Weight based dose (Median 65Kg)	195mg	\$3,592	\$824	45mg	\$93,392	\$21,424
Fixed-dose	240mg	\$4,416	NA	NA	\$114,816	NA

23-54 extra patients could be treated if the weight-based dose was used.

Immune-related adverse-events (IRAE)

- Approximately 10% to 50% of patients treated with immunotherapy will develop an IRAE.
- More than 90% of G3/4 IRAE will resolve with high-dose steroids.
- Timely identification and timely treatment are key.

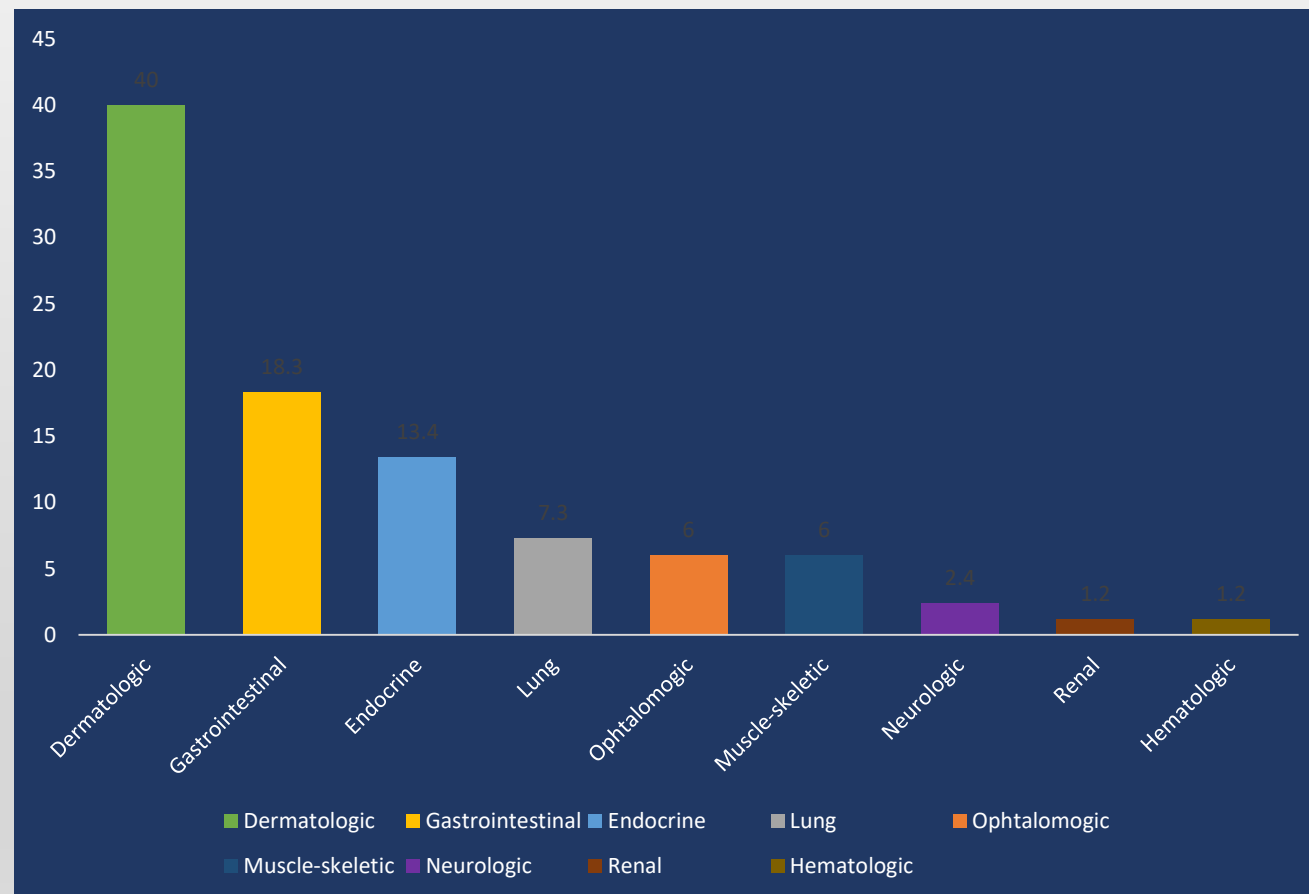


Incidence of IRAE's. Mexico's experience

- Multicentric retrospective study
- 140 patients with different primary tumors

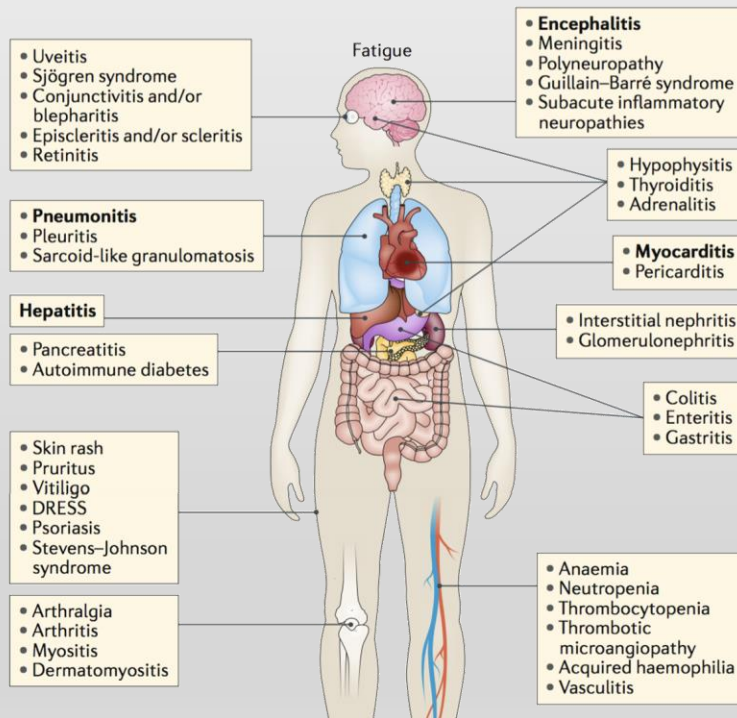
G3/4 IRAE's

- Nivolumab/Ipilimumab 33.3%
- Pembrolizumab 17.4%
- Ipilimumab 10%
- Nivolumab 5.6%



Things I like to remember about IRAE's

1. Any system can be affected.



2. Several management guidelines available

ASCO

ESMO

NCCN

SITC

3. When in doubt, consult another colleague

More experienced oncologist

Another specialist

4. Team up!

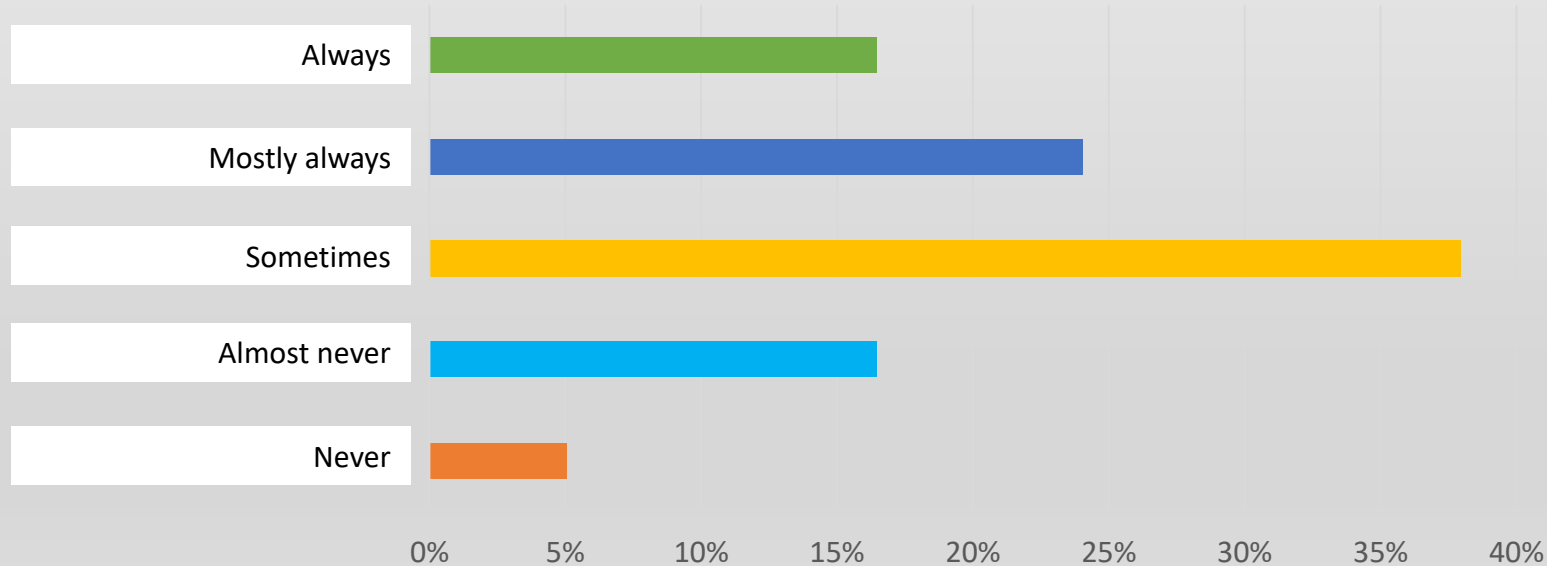
Identify those colleagues that are willing to learn and help the patient

5. Do not delay treatment for IRAE's

Do oncologists in Mexico team up?

- National Survey on immunotherapy access 2020.

How often do medical oncologists get other specialty consult when managing an IRAE?



Specialty consult	Number (%) (N=79)
Endocrinology	55.13
Dermatology	44.87
Internal Medicine	21.79
Gastroenterology	20.51
Nephrology	20.51
Rheumatology	14.10
Neurology	11.54
Cardiology	8.97
Other	19.23

Some patient's characteristics that should be identified before starting treatment.

- Where does my patient come from?
- What level of education does my patient have?
- Will I be able to reach my patient in case of an emergency?
- Which are my patient's ways of communication
 - Phone.
 - SMS.
 - Email.
- All patients and their caregivers need education!!!

Some areas of opportunity for expanding immunotherapy access in Mexico

- **Investigator initiatives**

- Cervical cancer
- Triple negative breast cancer
- Acral melanoma
- Gastric cancer

- **Local clinical guidelines**

In summary

- We are still lacking: Universal access, universal experience, more investigator-initiated clinical trials.
- But...
- Patients are already having the benefit of immunotherapy drugs.
- Medical oncologists throughout the country are having experience with immunotherapy drugs.
- Clinical trials are running in different parts of the country, expanding access throughout Mexico.
- An effort must be made to create areas of opportunity to expand access to immunotherapy.



Thank you!

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