FUNDACION BAMBERG

CICLO DE CONFERENCIAS
SOBRE ESTRATEGIAS E
INNOVACIÓN FRENTE AL CÁNCER

Avances Tecnológicos y Gestión
Asistencial Frente al Cáncer

¿Por qué necesitamos insistir en la investigación traslacional y en la investigación académica?

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Incidencia USA 2009

Estimated New Cases*

Males				Females		
Prostate	192,280	25%		Breast	192,370	27%
Lung & bronchus	116,090	15%		Lung & bronchus	103,350	14%
Colon & rectum	75,590	10%		Colon & rectum	71,380	10%
Urinary bladder	52,810	7%		Uterine corpus	42,160	6%
Melanoma of the skin	39,080	5%		Non-Hodgkin lymphoma	29,990	4%
Non-Hodgkin lymphoma	35,990	5%		Melanoma of the skin	29,640	4%
Kidney & renal pelvis	35,430	5%		Thyroid	27,200	4%
Leukemia	25,630	3%		Kidney & renal pelvis	22,330	3%
Oral cavity & pharynx	25,240	3%		Ovary	21,550	3%
Pancreas	21,050	3%		Pancreas	21,420	3%
All Sites	**766,130**	**100%**		**All Sites**	**713,220**	**100%**

A. Jemal. CA Cancer J. Clin. 2009

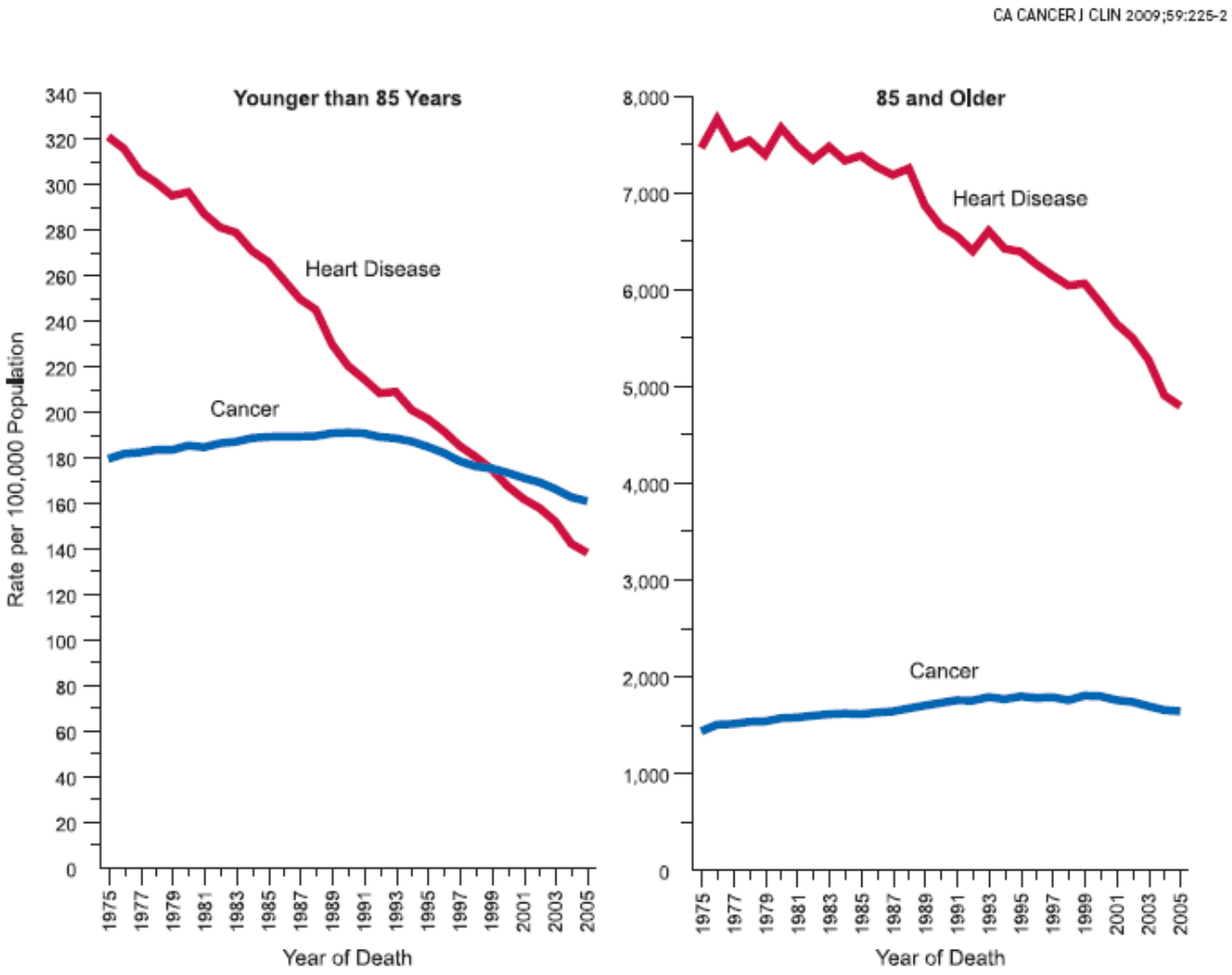
Mortalidad USA 2009

Estimated Deaths

Males				Females		
Lung & bronchus	88,900	30%		Lung & bronchus	70,490	26%
Prostate	27,360	9%		Breast	40,170	15%
Colon & rectum	25,240	9%		Colon & rectum	24,680	9%
Pancreas	18,030	6%		Pancreas	17,210	6%
Leukemia	12,590	4%		Ovary	14,600	5%
Liver & intrahepatic bile duct	12,090	4%		Non-Hodgkin lymphoma	9,670	4%
Esophagus	11,490	4%		Leukemia	9,280	3%
Urinary bladder	10,180	3%		Uterine Corpus	7,780	3%
Non-Hodgkin lymphoma	9,830	3%		Liver & intrahepatic bile duct	6,070	2%
Kidney & renal pelvis	8,160	3%		Brain & other nervous system	5,590	2%
All Sites	**292,540**	**100%**		**All Sites**	**269,800**	**100%**

A. Jemal. CA Cancer J. Clin. 2009

Mortalidad por cáncer y cardiovascular en USA según edad



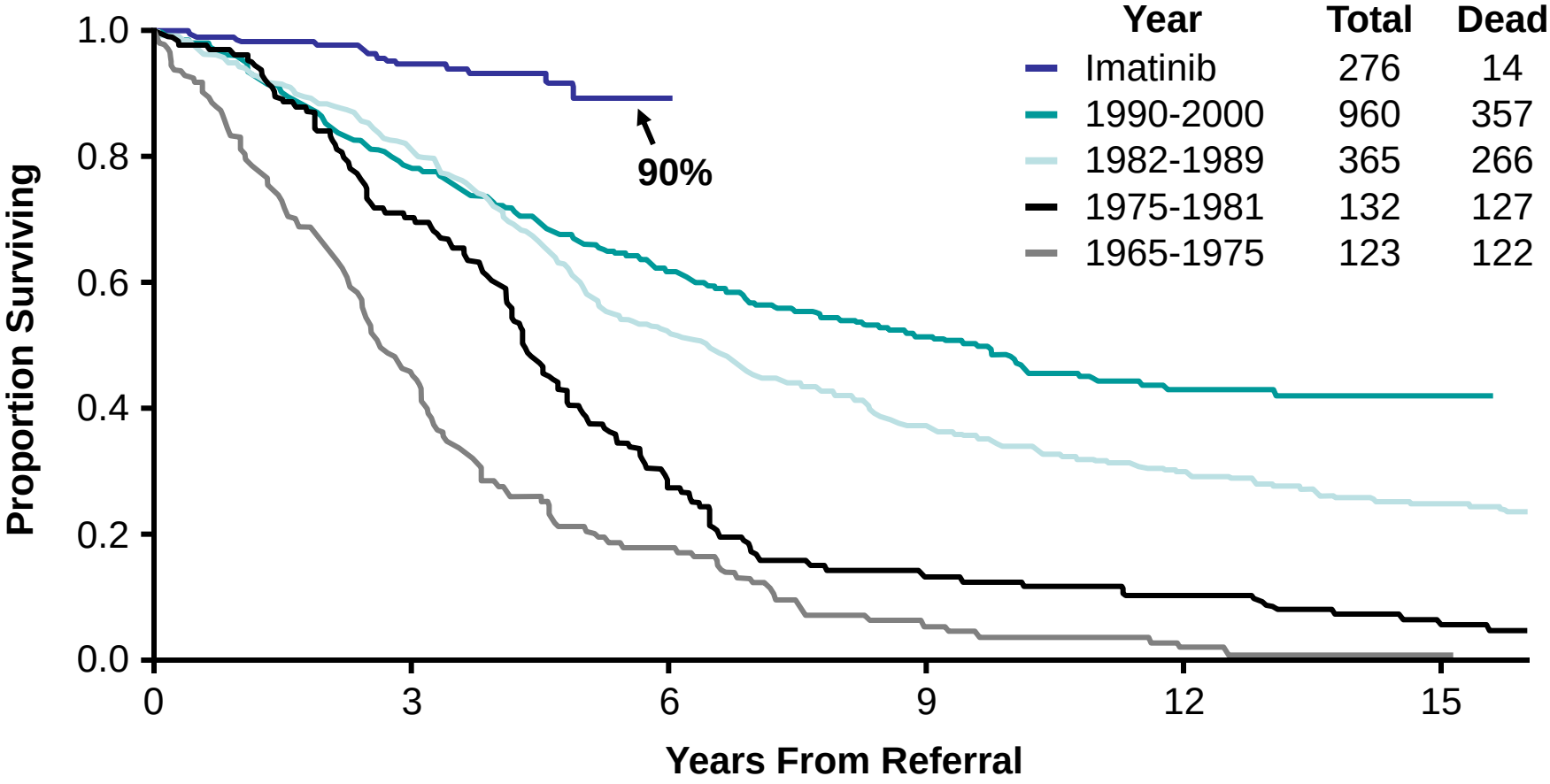
A. Jemal. CA Cancer J. Clin. 2009

Novel agents for cancer therapy

- Cellular signal transduction pathways
- Tumor vasculature
  - Angiogenesis inhibitors
  - Vascular disrupting agents
- Epigenetic modulators
- Targeting integrins
- Heat shock protein
- Ubiquitin-proteasome system
- Direct apoptosis enhancers
- PARP inhibitors
- Mitotic kinase inhibitors

Ma and Adjei 2009

Survival in Early Chronic-Phase CML



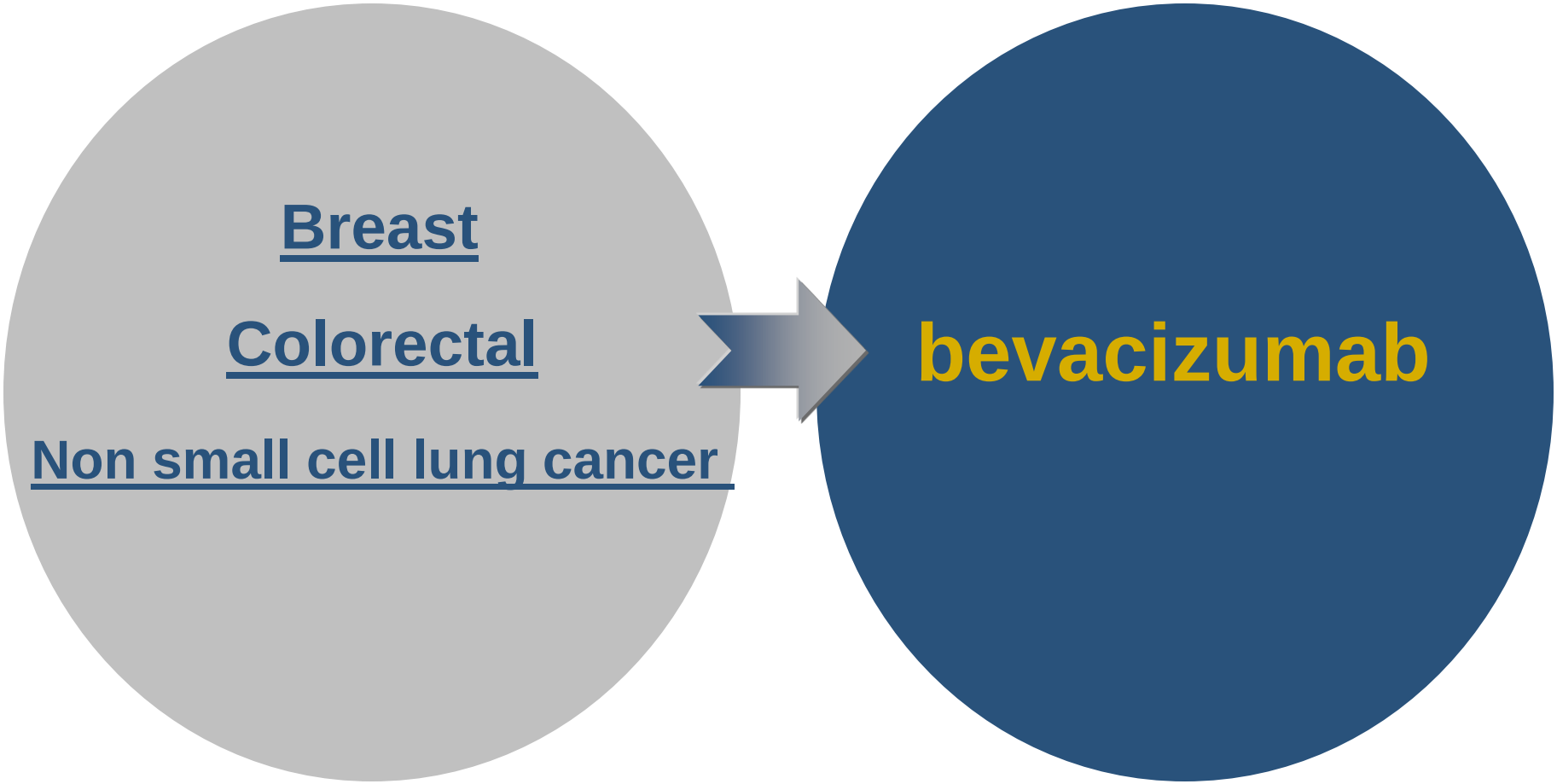
The University of Texas M. D. Anderson Cancer Center database.

Qué es lo que nos cuesta hacer y en qué tenemos que insistir

Investigación traslacional

Investigación clínica independiente

Antiangiogenic treatments approved in some types of tumours



Characteristics of antiangiogenic treatment

- ✓Modest impact in response rate (relevant?)
- ✓Modest impact in time to progression
- ✓Not relevant impact in overall survival
- ✓Moderate toxicity burden
- ✓Expensive

Potential Predictive Factors (Today!)

1. Circulating cytokines
2. CECs and CEPs
3. Genomics tools
4. Vascular imaging techniques

- DCE-MRI
- Dynamic CT scan
- Functional ultrasounds
- PET scan

SOME DATA ABOUT CYP2D6

- 20-25% of drugs are metabolized by CYP2D6.
- 101 known variants (26 null alleles).
- 7-10% spanish population ultrarapid metabolizers.
- Inhibitors:

  Amiodarone, chlorpheniramine, cimetidine, clomipramine, duloxetine, fluoxetine, paroxetine, haloperidol, methadone, ritonavir, quinidine.

- Inducers:

  Dexamethasone, rifampin.

Association between CYP2D6 polymorphisms and outcomes among women with early stage breast cancer treated with tamoxifen

Metabolizers	N	Relapse @ 9 ys	TTR HR (95% CI)
Extensive 2 functional alleles	609	14.9%	
Heterocygous (extensive / intermediate)	637	20.9%	1.40 (1.04-1.90)
Poor 2 non-functional alleles	79	29%	1.90 (1.10-3.28)

JAMA. 2009 Oct 7;302(13):1429-36

Deaths in aromatase inhibitor trials

Table 1. No. of Deaths According to Type of Hormone Treatment

Trial	No. of Patients	Treatment	Follow-Up (months)	No. of Deaths	HR for OS	*P*
First-line						
ATAC[5]	6,241	A = 3,125 *v* T = 3,116	100	A = 629 T = 624	0.97	.7
BIG 1-98[8]	4,922	L = 2,463 *v* T = 2,459	76	L = 303 T = 343	0.87	.08
TEAM[7]	9,775	E = 4,898 *v* T = 4,868	33	E = 88 T = 82	NA	
Sequential						
IES[4]	4,724	E = 2,352 *v* T = 2,372	55.7	E = 222 T = 261	0.85 0.83*	.08 .05
ABCSG8/ARNO95[6]	3,224	A = 1,618 *v* T = 1,606	28	A = 45 T = 59	NA	.16
ITA[3]	448	A = 223 *v* T = 225	36	A = 12 T = 21	NA	.1

Abbreviations: HR, hazard ratio; OS, overall survival; ATAC, Arimidex, Tamoxifen Alone, or in Combination; A, anastrozol; T, tamoxifen; BIG, Breast International Group; L, letrozole; E, exemestane; TEAM, Tamoxifen Exemestane Adjuvant Multinational; NA, not available; IES, Intergroup Exemestane Study; ABCSG, Austrian Breast and Colorectal Cancer Study Group; ARNO, Arimidex-Nolvadex; ITA, Italian Tamoxifen Anastrozole.

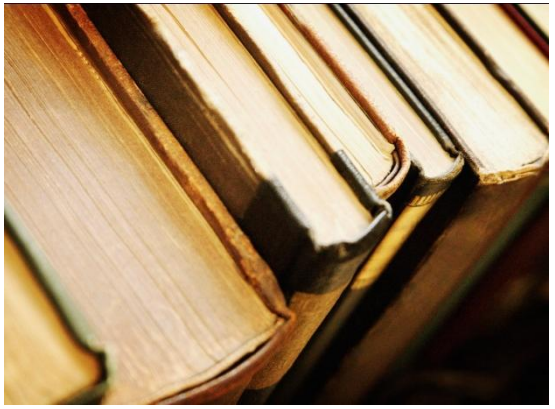
*Subanalysis excluding patients with estrogen receptor–negative disease.

Sanchez- Muñoz et al. JCO 2009

La necesidad de la investigación académica

Es fácil investigar fármacos

Es difícil investigar conceptos

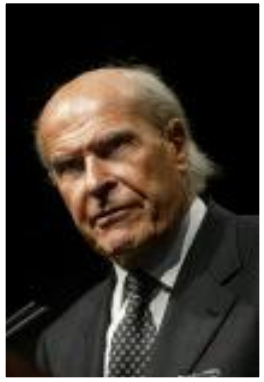


RESULTADOS DE LOS TRATAMIENTOS LOCALES EN EL CÁNCER DE PROSTATA

tratamiento	Sup.10 años	Sup. 15 años	% recaídas locales
Prostatectomía radical	92-97%	86-94%	15-20%
radioterapia	65-86%	60-65%	15-20%

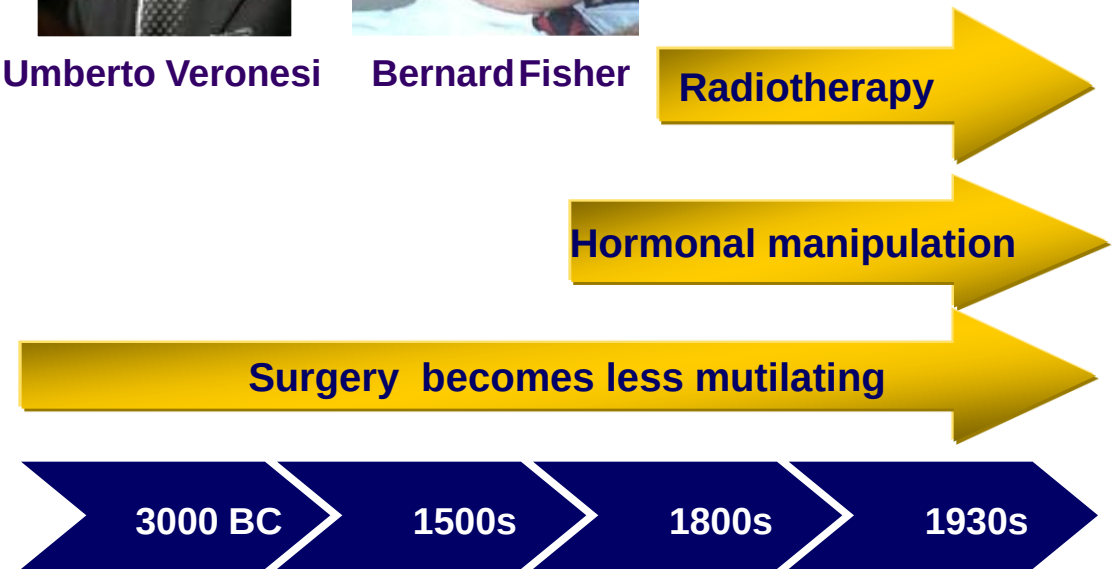
Los resultados entre tratamientos son difícilmente comparables, ya que los pacientes tratados con radioterapia suelen partir de un peor estado general y suelen ser estadios más avanzados

The success of radiotherapy leads to the concept of conservative surgery



Umberto Veronesi

Bernard Fisher



- In the 1920s and 1930s pioneering investigators, such as Keynes in England, Peters in Canada, Baclesse in France, and Mustakallio in Finland, began to treat groups of women with breast-conserving partial mastectomies followed by irradiation to the intact breast, challenging the need for total mastectomy.
- This ultimately led to the use of breast-conserving surgery, rather than mastectomy.

CONCLUSIONES

- El cáncer es un problema importante de salud (como algunos otros).
- La investigación traslacional necesita la creación de estructuras organizativas que posibiliten su desarrollo optimo.
- La investigación clínica académica es necesaria para resolver problemas de salud diferentes a la comercialización de nuevos farmacos.
- No avanzaremos de forma óptima en la lucha contra el cáncer sin un apoyo decidido a la investigación traslacional y a la investigación clínica académica.