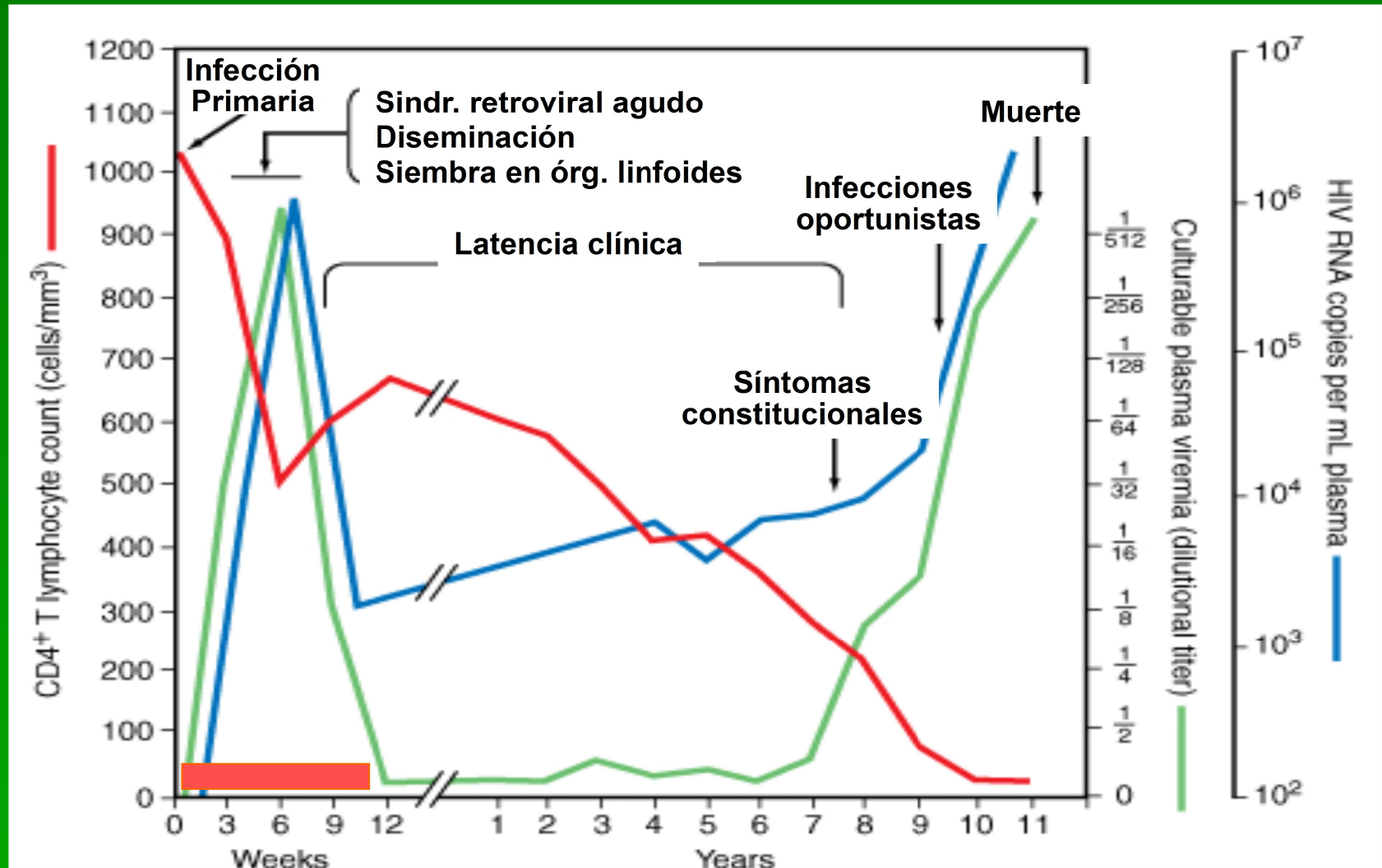




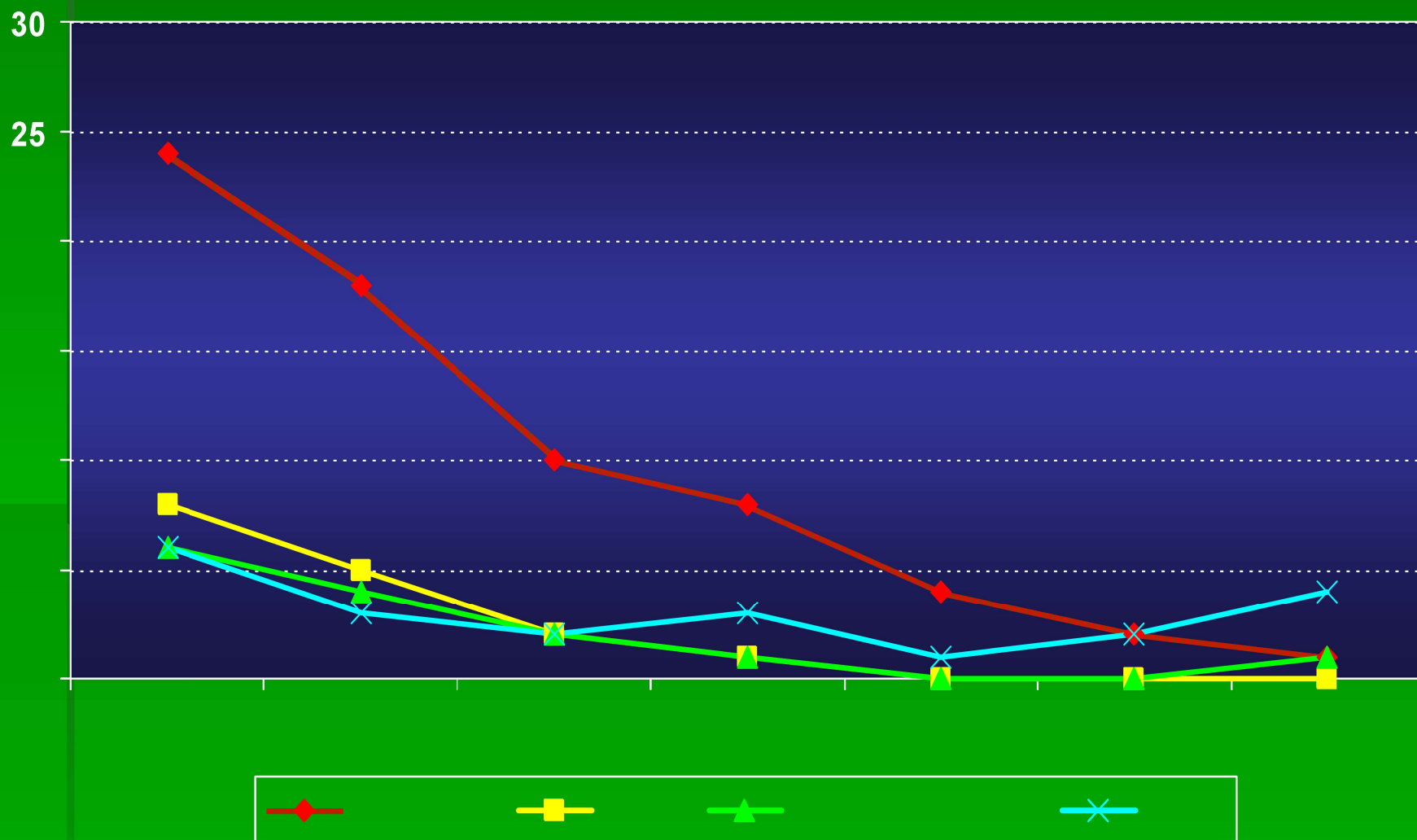
El VIH en Urgencias



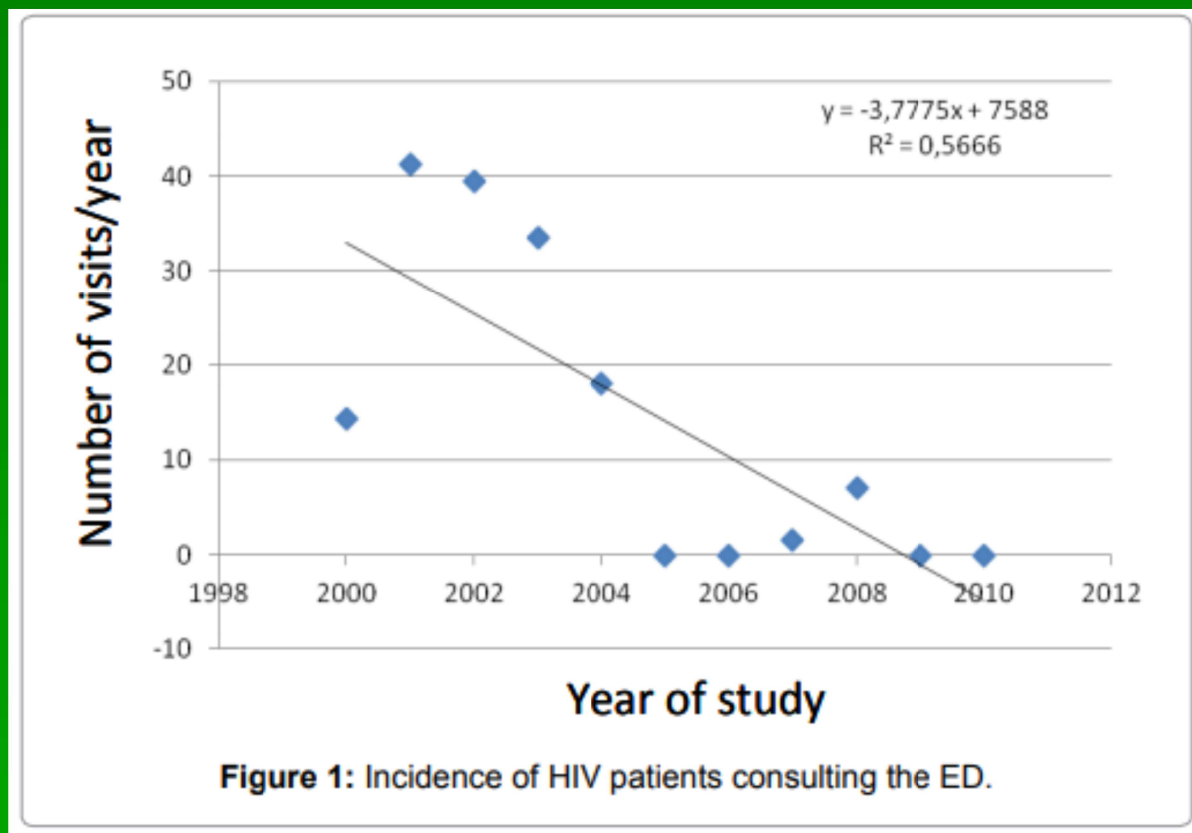
Ernesto Martínez B., MD
Internista Infectólogo
Presidente de REVIVA
Profesor Universidad del Valle



I .O. Durante H A A R T



Reason for HIV Patients Consultation to the Emergency Department in the HAART Era (Barcelona, N = 445, 2014)



Reason
Depa

emergency
ña – 2016)

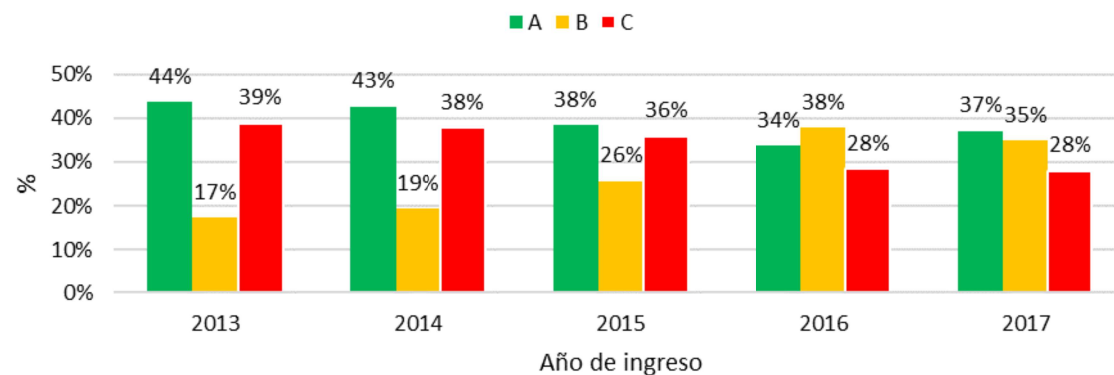
Diseases	Frequency	Percentage (%)
Respiratory infection	135	30.3
Neurological disease	37	8.3
Fever	33	7.4
SNC infection	22	4.9
Osteomuscular disease	22	4.9
Digestive disease	21	4.7
Abdominal infection	20	4.5
Liver disease	19	4.3
Cardiovascular disease	18	4.0
Dermatological disease	18	4.0
Hematological disease	17	3.8
Oncologic disease	10	2.2
Constitutional syndrom	10	2.2
Kidney infection	8	1.8
Surgery	7	1.6
Pulmonary disease	6	1.3
Vascular disease	6	1.3
Lymphadenopathy	6	1.3
Bone infection	5	1.1
Psychiatric illness	5	1.1
Gynecological disease	4	0.9
Kidney disease	4	0.9
Endocarditis	4	0.9
Endocrinological disease	3	0.7
Ophthalmological disease	3	0.7
Drugs overdose	2	0.4
TOTAL	445	100

La realidad aún en Colombia:

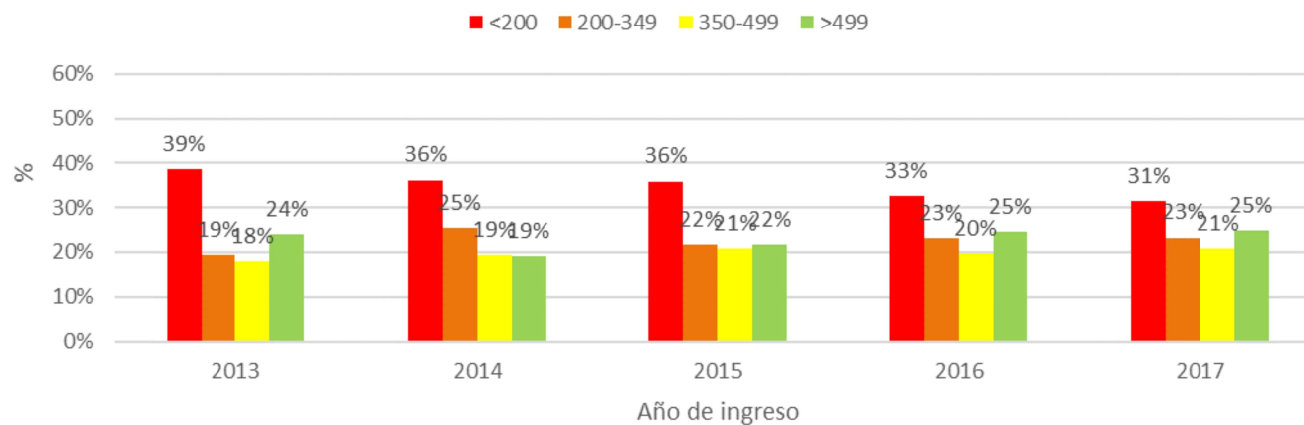
Estado CDC y recuento de CD4+ de los ingresos al Grupo VIHCOL, 2013 - 2017

N = 11280

Distribución cohorte total etapa CDC al ingreso al centro por año de ingreso



Distribución valor CD4 al ingreso al centro total cohorte por año de ingreso



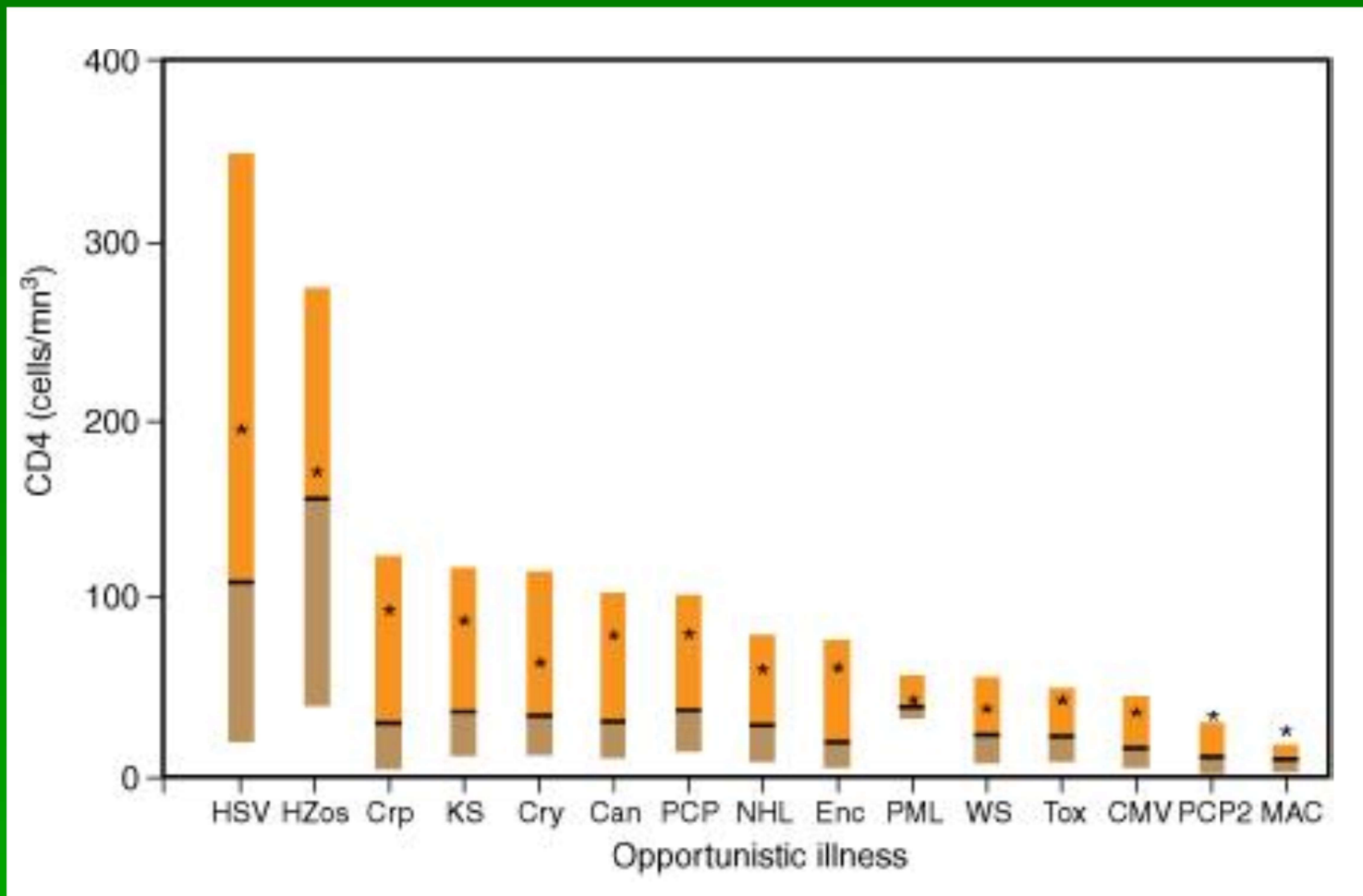
Infecciones oportunistas en pacientes con VIH en el hospital universitario de Neiva, Colombia. 2007-2012 ***N = 286***

Tabla 1 Métodos diagnósticos y etiología de infecciones oportunistas, HUHMP 2007-2012

	N.º Dx	Métodos diagnósticos										Casos documentados ^a (%)
		Imágenes (%)	PCR (%)	Aspirado (%)	ZN (%)	Cultivo (%)	LBA (%)	ADA (%)	Látex (%)	VDRL (%)	ZN Mod (%)	Biopsia
<i>Toxoplasma</i>	154	86	8	1								95
<i>Micobacterias</i>	92	60	3		17	2	12	5				100
<i>Cryptococcus</i> sp.	55	4							84			88
<i>Pneumocystis jirovecii</i>	43		14				81					95
<i>Cryptosporidium</i> sp.	27										100	100
Citomegalovirus	18		100									100
HSV	20		85									85
<i>Treponema pallidum</i>	17									100		100
<i>Histoplasma capsulatum</i>	16					32	38					95
<i>Candida</i>	102					3						3
<i>Aspergillus</i> sp.	1	100										100
<i>Mycobacterium leprae</i>	2				100							100
VPH	5										20	20

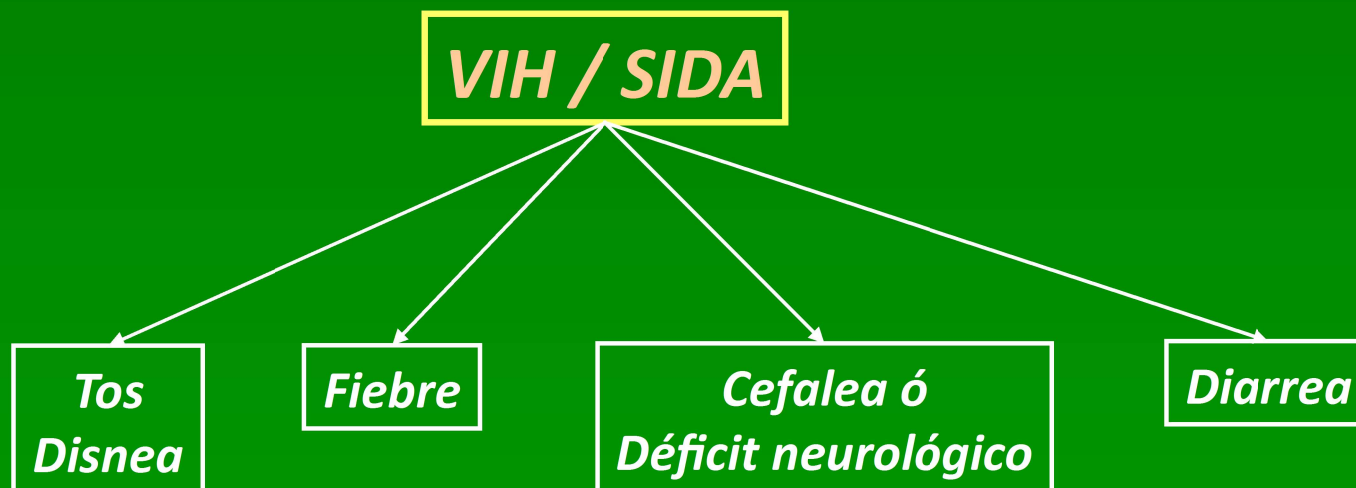
Relevante en la historia clínica :

- **Antecedentes de condiciones asociadas o no a SIDA**
- **Estado clínico general (Estado nutricional, Karnofski, BMI)**
- **Estado de inmunosupresión :**
 - Conteo de células CD4+ (> 200, <200, < 100, < 50)
 - Hemograma : Linfocitos totales < 1200 / mm³
- **Tratamiento antiretroviral :**
 - Inicio, duración (→ Recuperación inmune, SRI).
 - Medicamentos (→ Toxicidad, Rx alérgicas)
- **Factores epidemiológicos :**
 - Epidemiología local: TBC, criptococosis, histoplasmosis
 - Condiciones de higiene
 - Convivencia con mascotas
 - Agua potable
 - Hábitos sexuales: Pareja estable, uso de preservativo, contactos, etc.



Relación conteo de CD4+ y presencia de infecciones oportunistas

Por qué consulta un paciente seropositivo al servicio de urgencias ? . . .



Otras causas :

- *Brote*
- *Náuseas, vómito*
- *Alteraciones visuales*
- *Disfagia, odinofagia*
- *Ictericia*
- *Masa, adenopatías*

Tos
Disnea

- *Pneumocystis jiroveci*
- Neumonías bacterianas
- Tuberculosis
- Infecciones micóticas

Fiebre prolongada

Tos seca

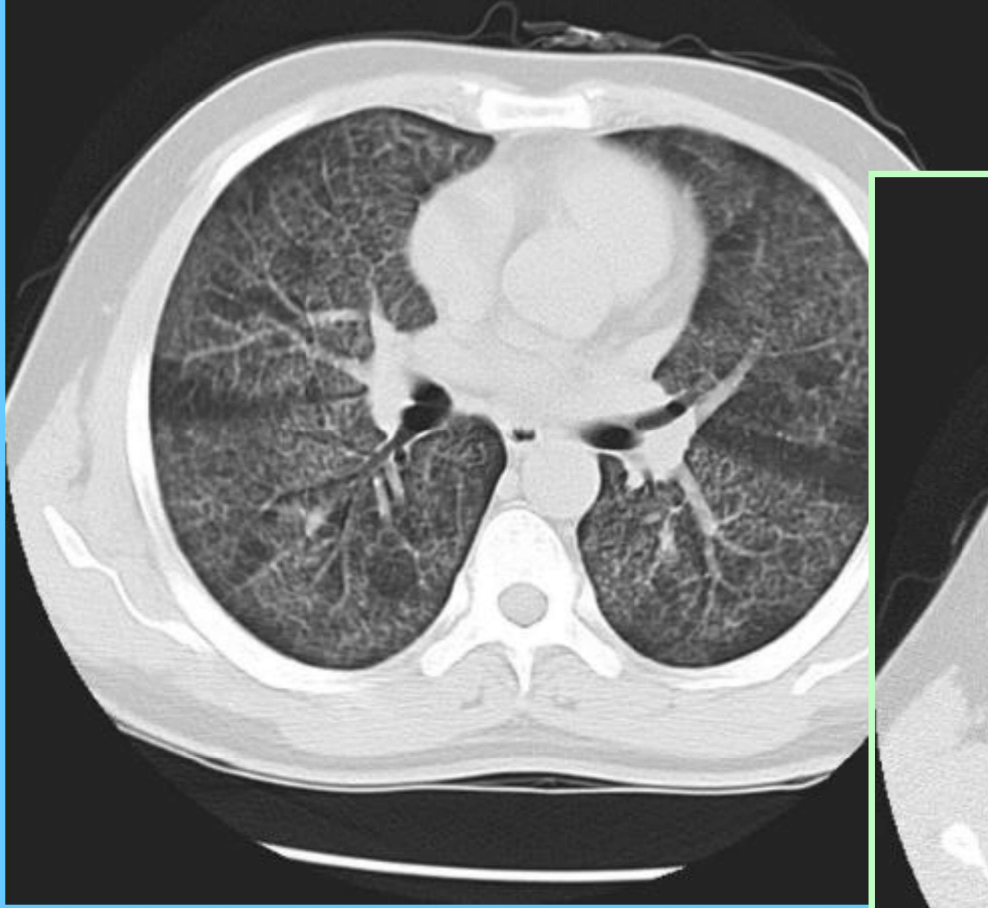
Disnea progresiva

Fatiga

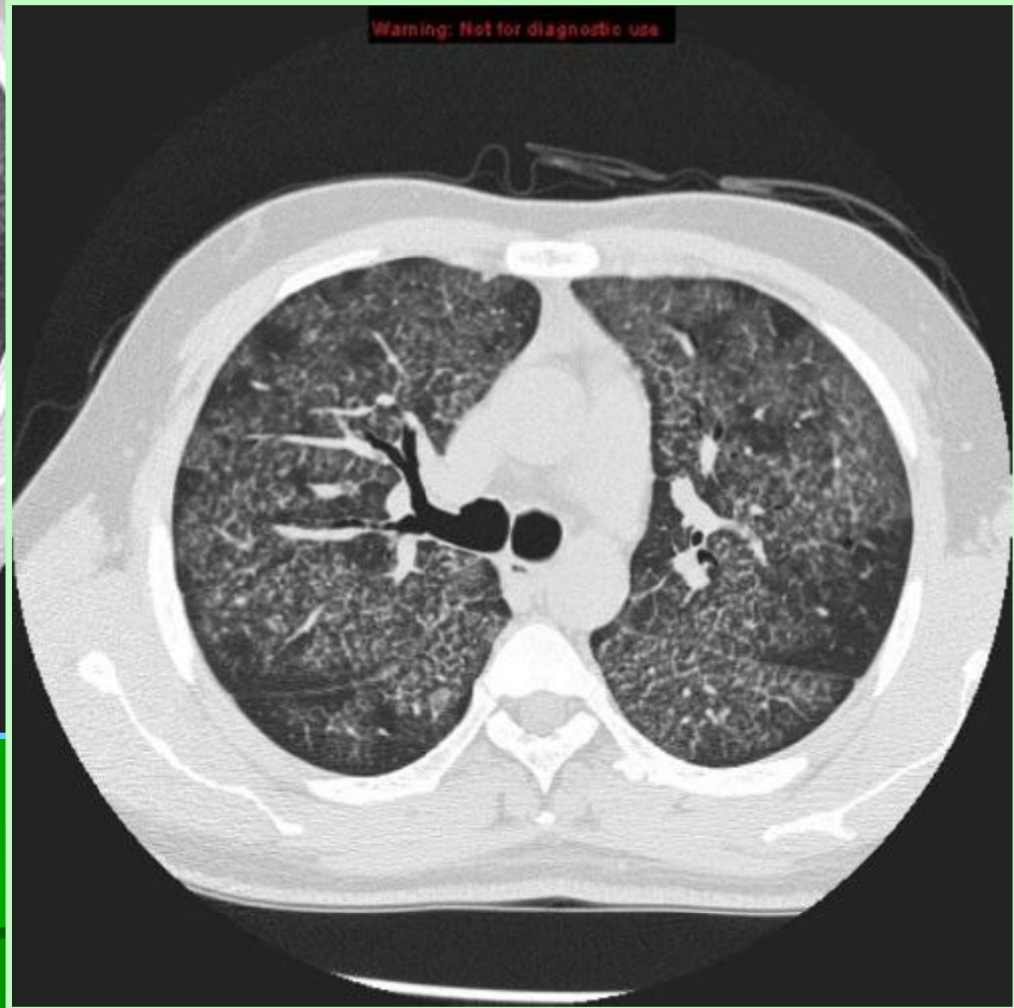
Ausencia de derrames



Warning: Not for diagnostic use



Warning: Not for diagnostic use



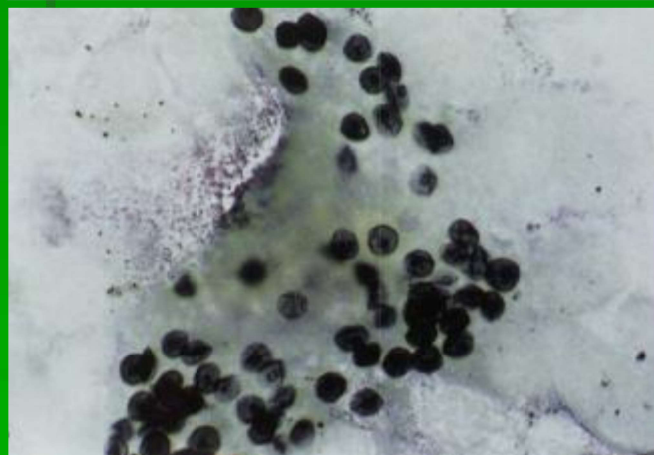
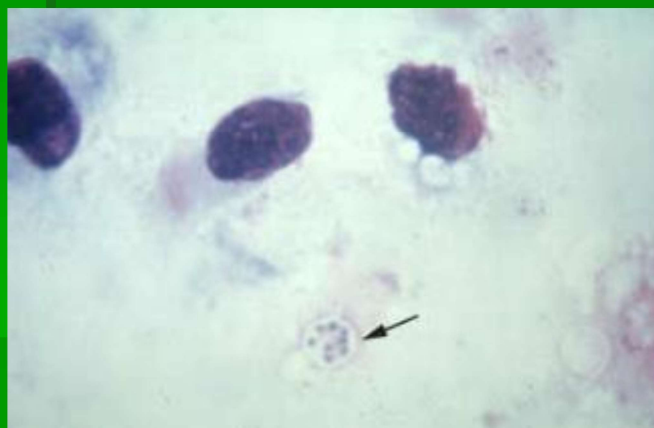
Fiebre prolongada

Tos seca

Disnea progresiva

Fatiga

Ausencia de derrames



- *Inducción de esputo*
- *Lavado broncoalveolar*
- *Coloraciones de plata metenamina*
- *PCR, β -2,3-glucano: Altamente prometedores*
- *LDH → Solo una guía, sirve como seguimiento*

<i>1a Línea</i>	<i>Alergia</i>	<i>Falla Terapéutica</i>
<i>Trimetoprim-Sulfa</i>	<i>Clindamicina + Primaquina</i>	<i>Pentamidina EV ???</i>
Leve	Moderada	Severa
pO₂ > 70, PAFI > 250 D(A-a) < 35 (a.a.)	pO₂ < 70, PAFI < 250 D(A-a) > 35 (a.a.)	
TMS oral (15 mg/Kg TMP) 21 d	TMS EV → Oral (20 mg/Kg TMP) 21 d	TMS EV + Esteroides (40 BID x 5 d 20 BID x 5 d 20 QD x 11 d)

Tos
Disnea

- *Pneumocystis jiroveci*
- Neumonías bacterianas
- Tuberculosis
- Infecciones micóticas

NEUMONIAS EN PACIENTES CON VIH/SIDA

CD4+ > 200

Neumonías bacterianas (NAC)

Str pneumoniae (B/mia 100 X)

H influenzae (5 – 6 X)

Salmonella

Moraxella catarrhalis

S aureus (4.6 %)

Mycoplasma

Chlamydia

Legionella

Tuberculosis

CD4+ < 200

PCP

Bacterias

Nocardia

**Pseudomonas - 2.3 %
(CD4+ < 50)**

Hongos

Cryptococo

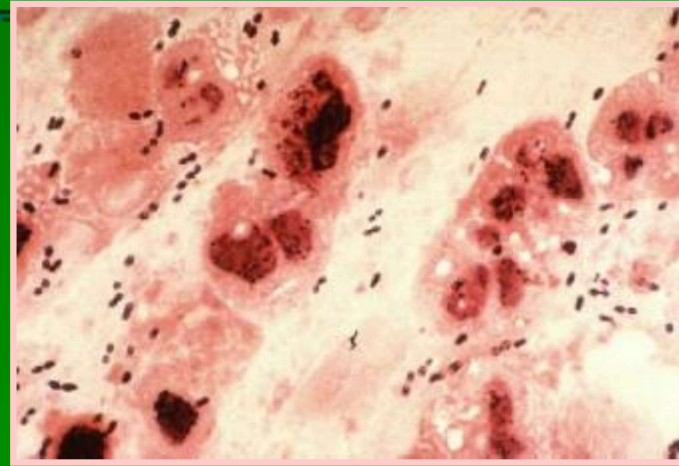
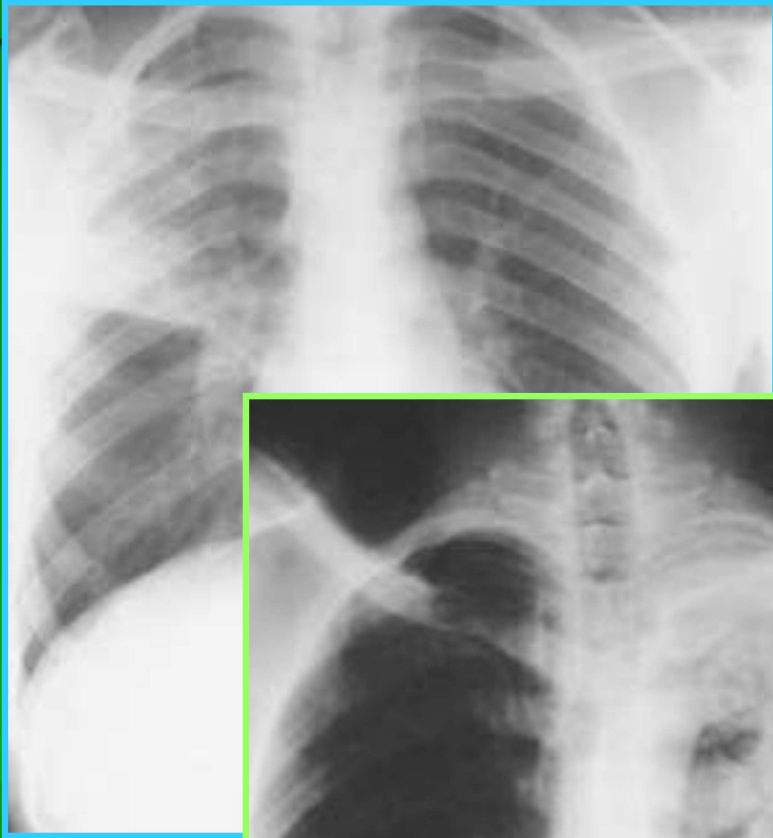
Histoplasma

Otros

Virus

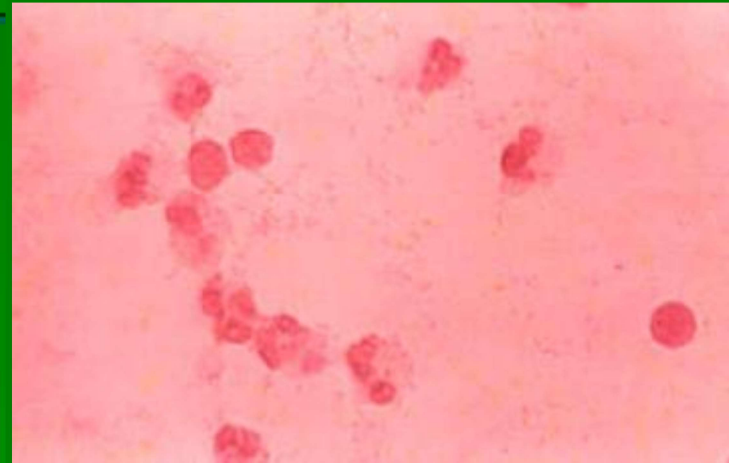
CMV





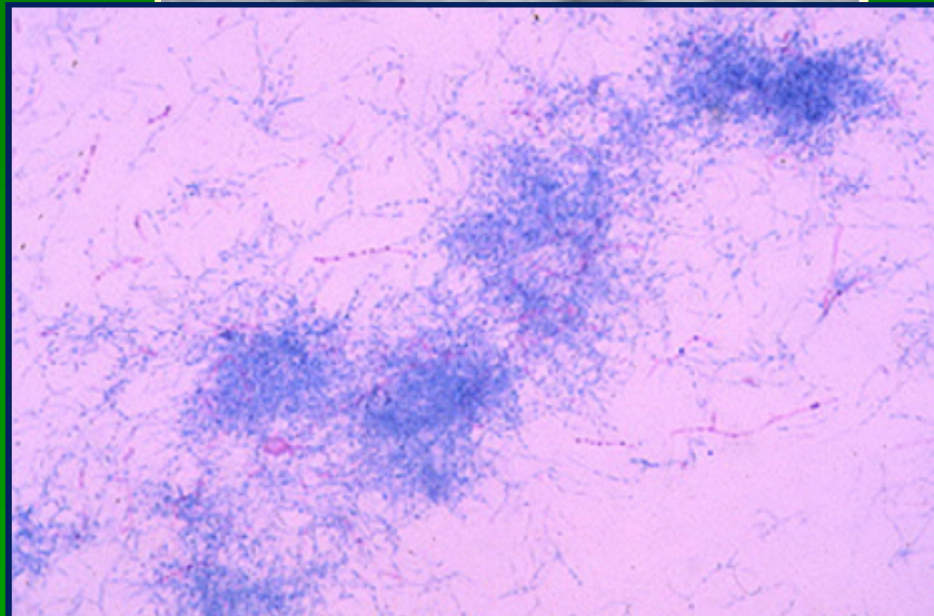
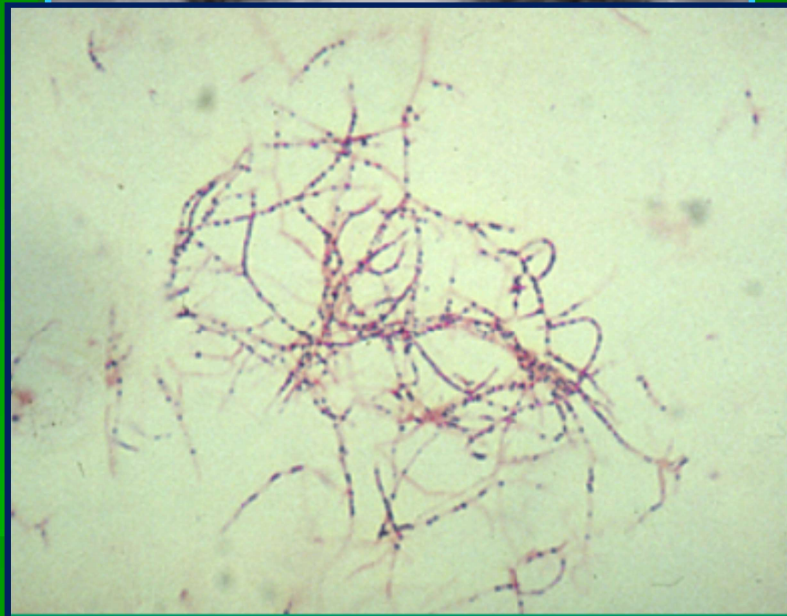
Str pneumoniae

- No SpRP en neumonía en Colombia
- Tto con penicilina o ampicilina



Haemophilus influenzae

- *Tasa baja de productor de betalactamasas*
- *Tto con ampicilina usualmente ok*



Nocardia asteroides

- Tto con TMS (15 mg/Kg/d) + meropenem x 3-4 sem, luego TMS – 10 mg/Kg/d VO hasta 6 meses.



Tos
Disnea

- *Pneumocystis jiroveci*
- Neumonías bacterianas
- Tuberculosis
- Infecciones micóticas

Tuberculosis – Cuadro clínico

PRIMOINFECCION

REACTIVACION

TBC MILIAR (DISEMINADA)

Cualquier CD4+



PRIMOINFECCION

REACTIVACION

TBC MILIAR (DISEMINADA)

CD4+ > 200

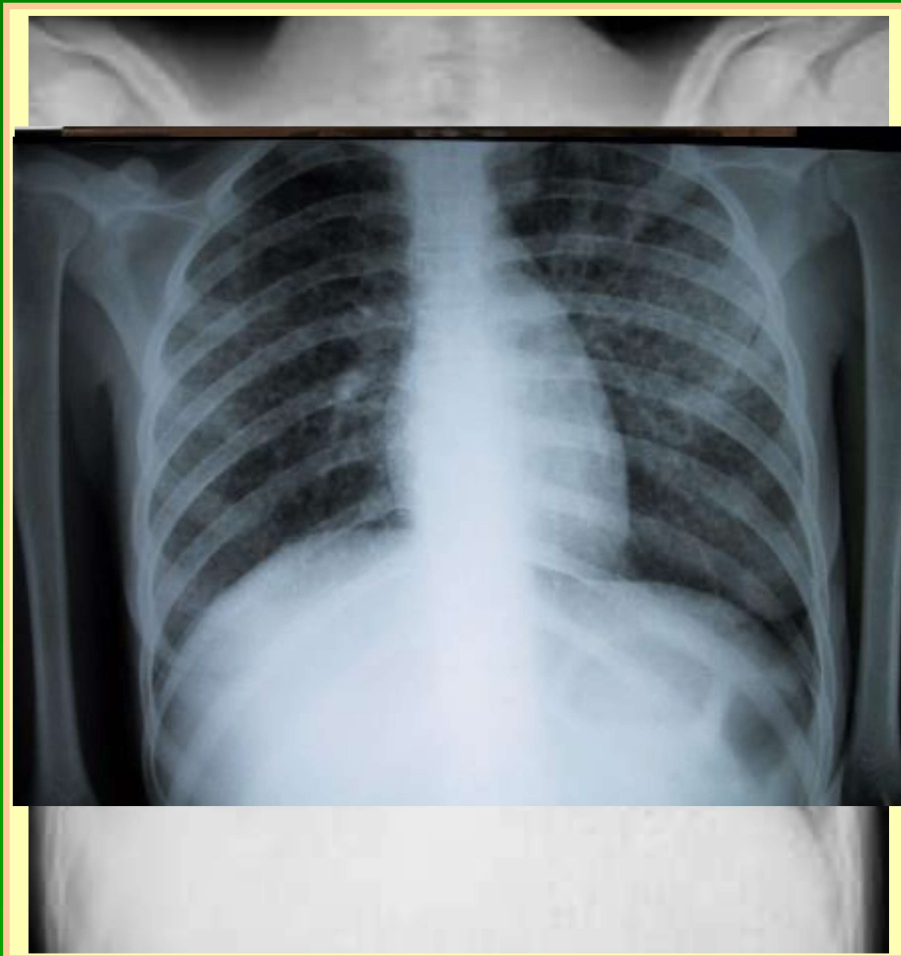


PRIMOINFECCION

REACTIVACION

TBC MILIAR (DISEMINADA)

CD4+ < 200

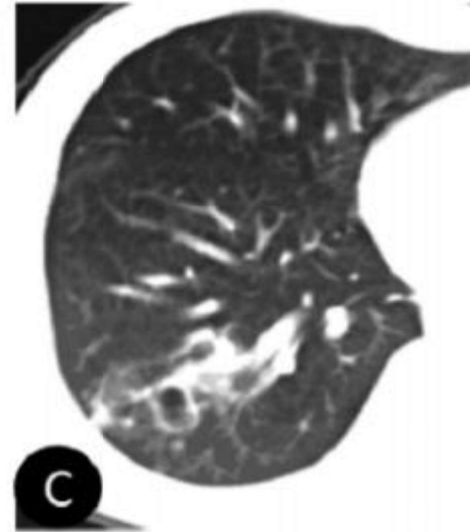
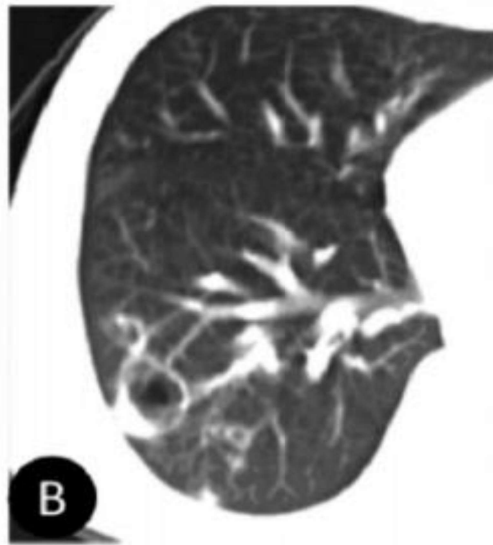


Tratamiento de tuberculosis en VIH

	<i>TB pulm multiS</i>	<i>TB disem.</i>
<i>1a Fase</i>	<i>RIPE x 2 m</i>	<i>RIPE x 2 m</i>
<i>2a Fase</i>	<i>RI x 4 - 7 m</i>	<i>RI x 7 m</i>
<i>Con HAART</i>	<i>EFV o RAL + TDF/FTC</i>	

Tos
Disnea

- *Pneumocystis jiroveci*
- Neumonías bacterianas
- Tuberculosis
- Infecciones micóticas

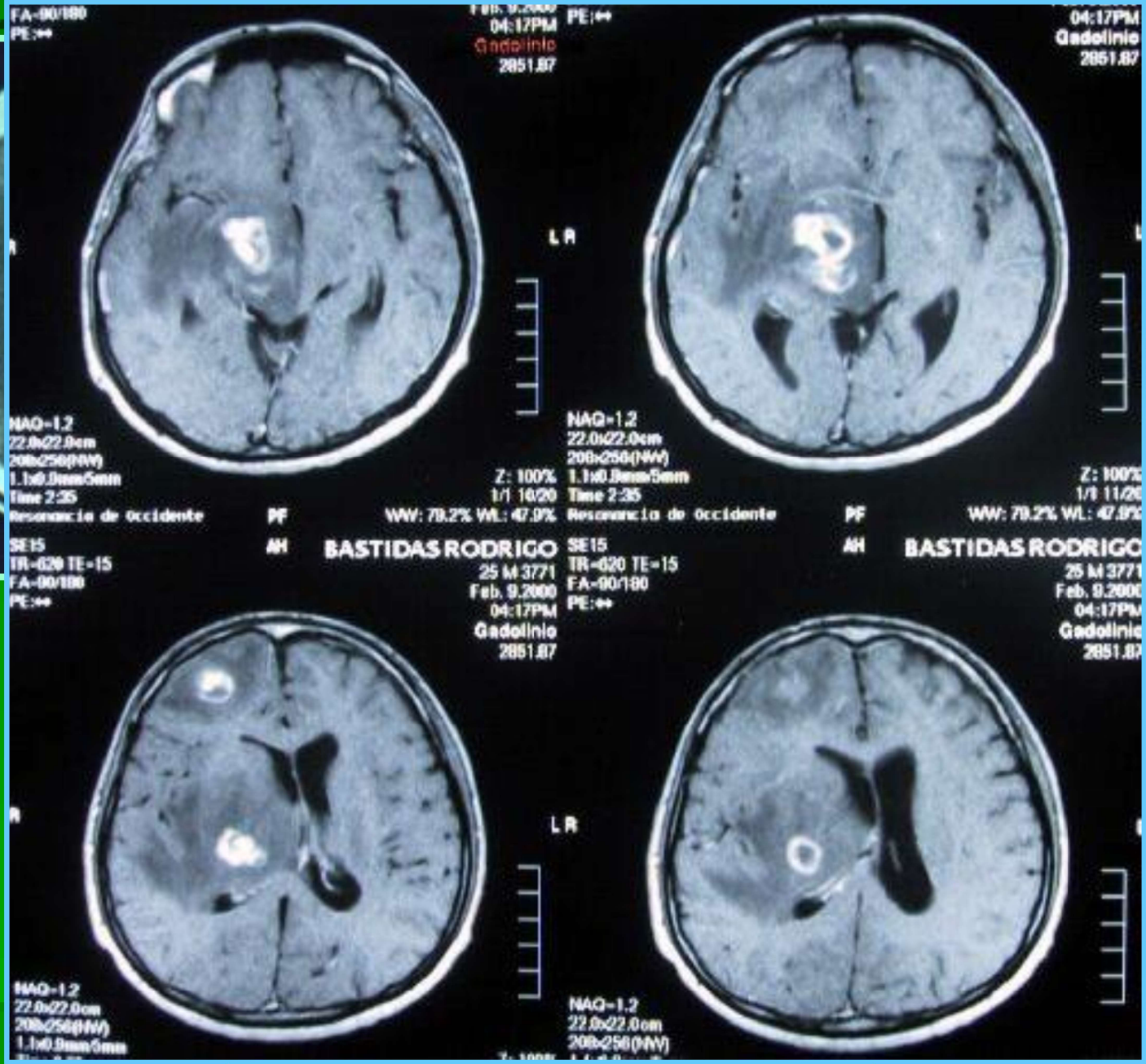
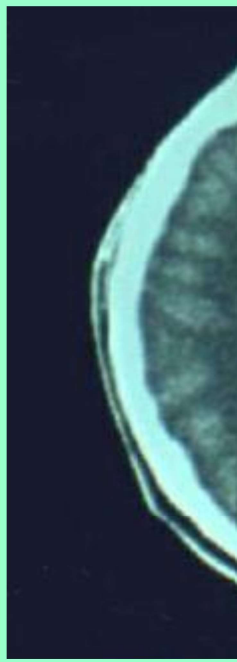


Neumonía cryptocóccica: Tto: Fluconazol ó AnfoB

Cefalea
Alteraciones
neurológicas

- Toxoplasmosis
- Cryptococosis
- Tuberculosis

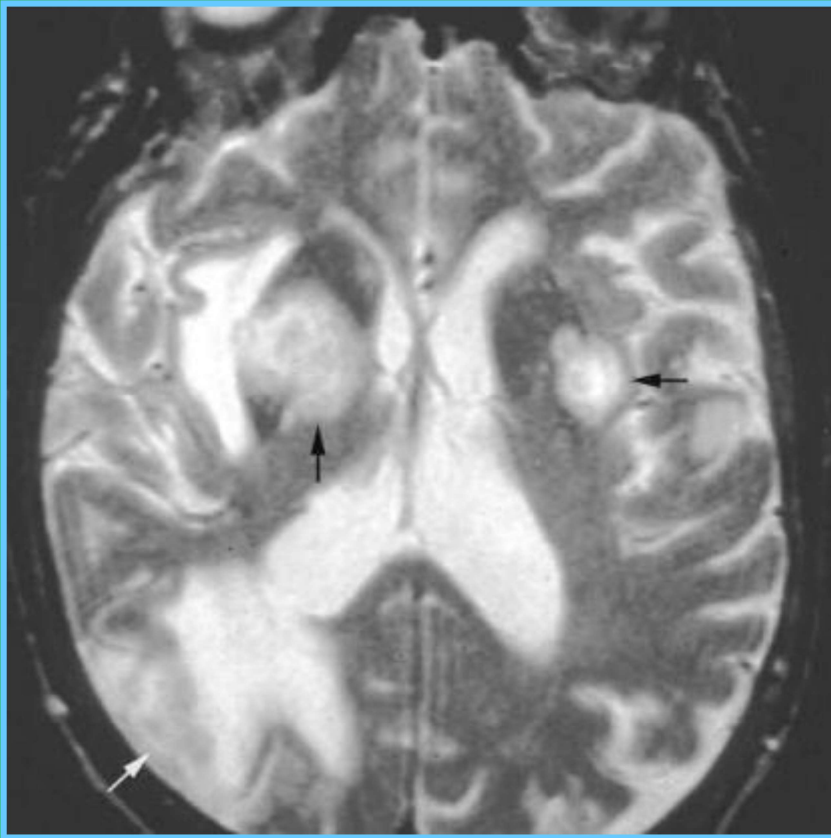
El VIH en el servicio de urgencias . . .



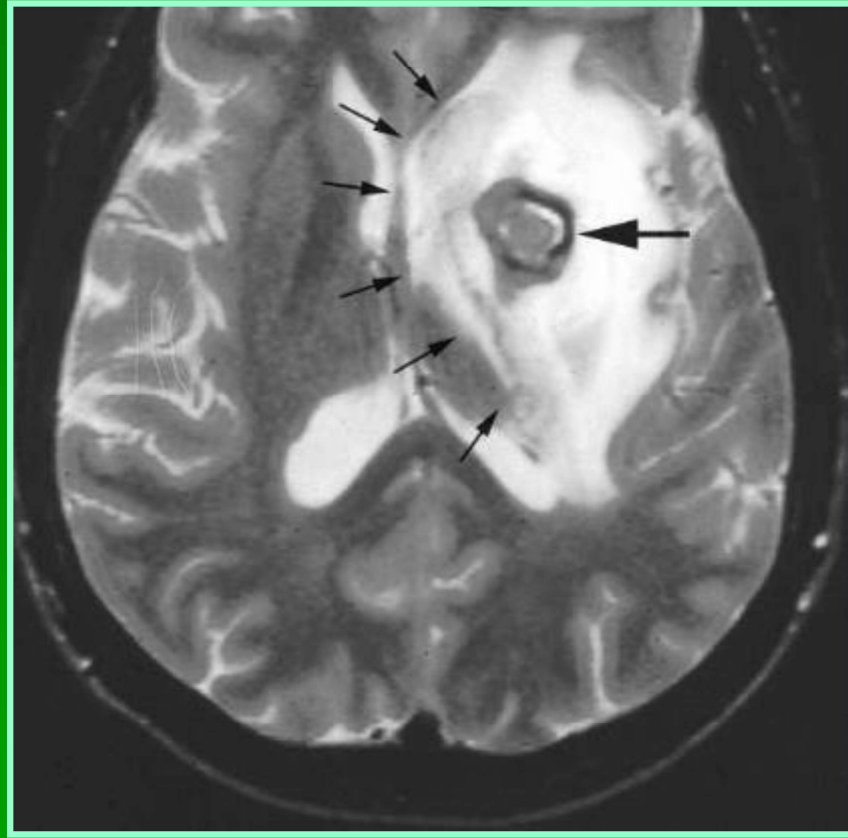
TOXOPLASMOSIS

- 50 – 70 % de lesiones focales en SN C
- 60 - 70 % son múltiples
 - Ganglios basales
 - L óbulos frontales
 - L óbulos temporales
 - Sustancia blanca o gris subcortical
- TA C vs R N M :
 - Más sensible
 - Influye en actitud terapéutica
 - En 6 casos documentados por biopsia:
 - * Por TA C : 3 sin lesiones
1 con lesión única
 - * Por R N M : 6 / 6 lesiones múltiples
 - Si lesión única por R N M → linfoma 70 %

RESONANCIA MAGNETICA



Toxo cerebral



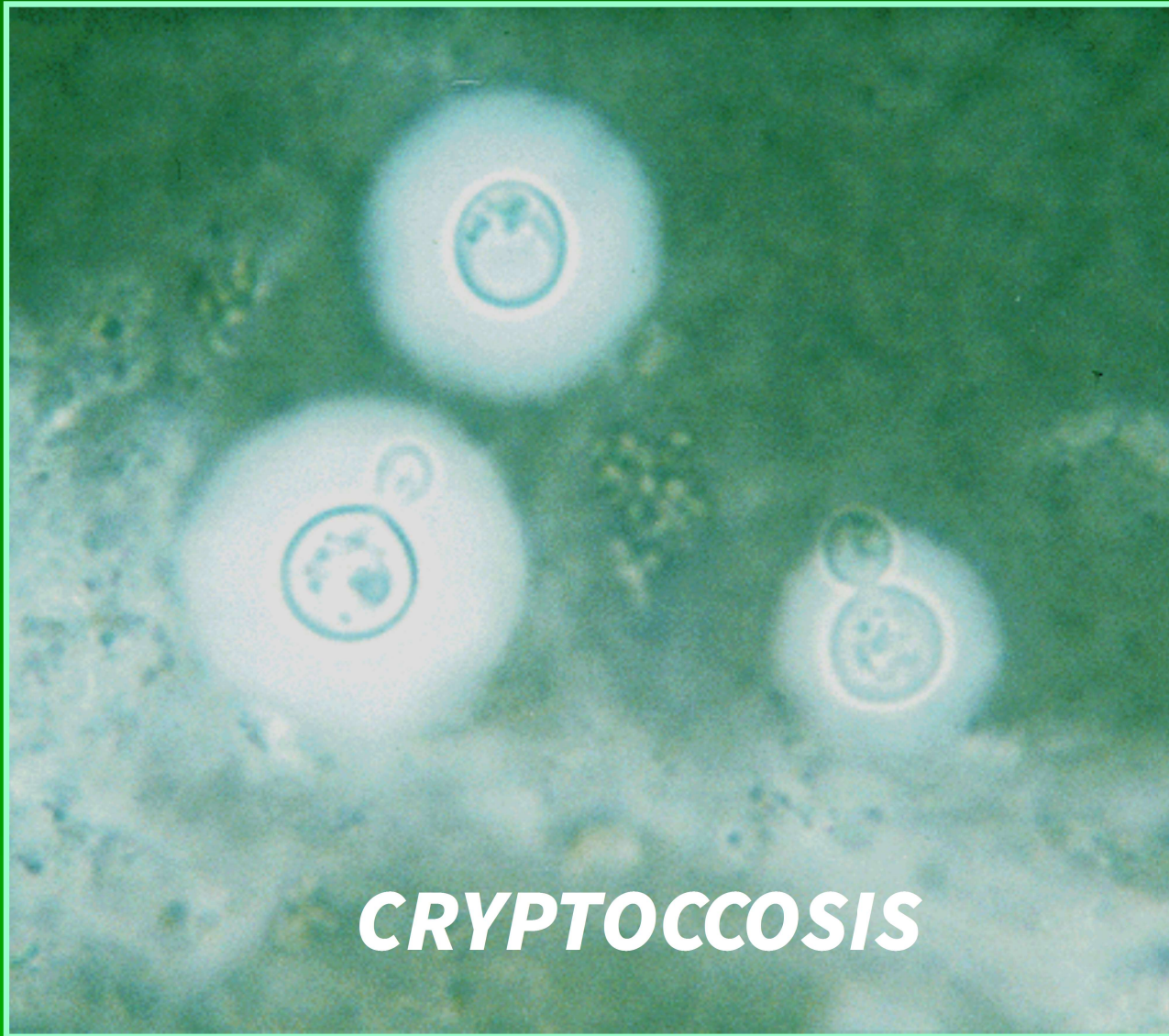
Linfoma SNC

TOXOPLASMOSIS

- *Diagnóstico serológico :*
 - *I gG (+) : A riesgo, no diagnóstica*
 - *I gG (-) : No la excluya pero piense en otro Dx*
 - *I gM (Suero) : Escasa utilidad*
 - *I gG ó I gM en LCR : Sólo (+) en 30 – 60 %*
 - *PCR en LCR : S = 60 – 70% E = 100%*

TOXOPLASMOSIS

- *El dilema terapéutico en Colombia:*
 - Disponibilidad escasa de Sulfadiazina y Pirimetamina
 - No disponemos de Atovaquona
 - Monoterapia con TMS: falta de evidencia sólida
- *Opciones:*
 - Clindamicina – 600 – 1200 mg cada 6 horas + ?...
 - Azitromicina – 500 – 1000 mg/d
 - Claritromicina – 1000 mg/d
 - ? Clindamicina + TMS-ev. . .
 - ? Esteroides . . .



CRYPTOCOCOSIS

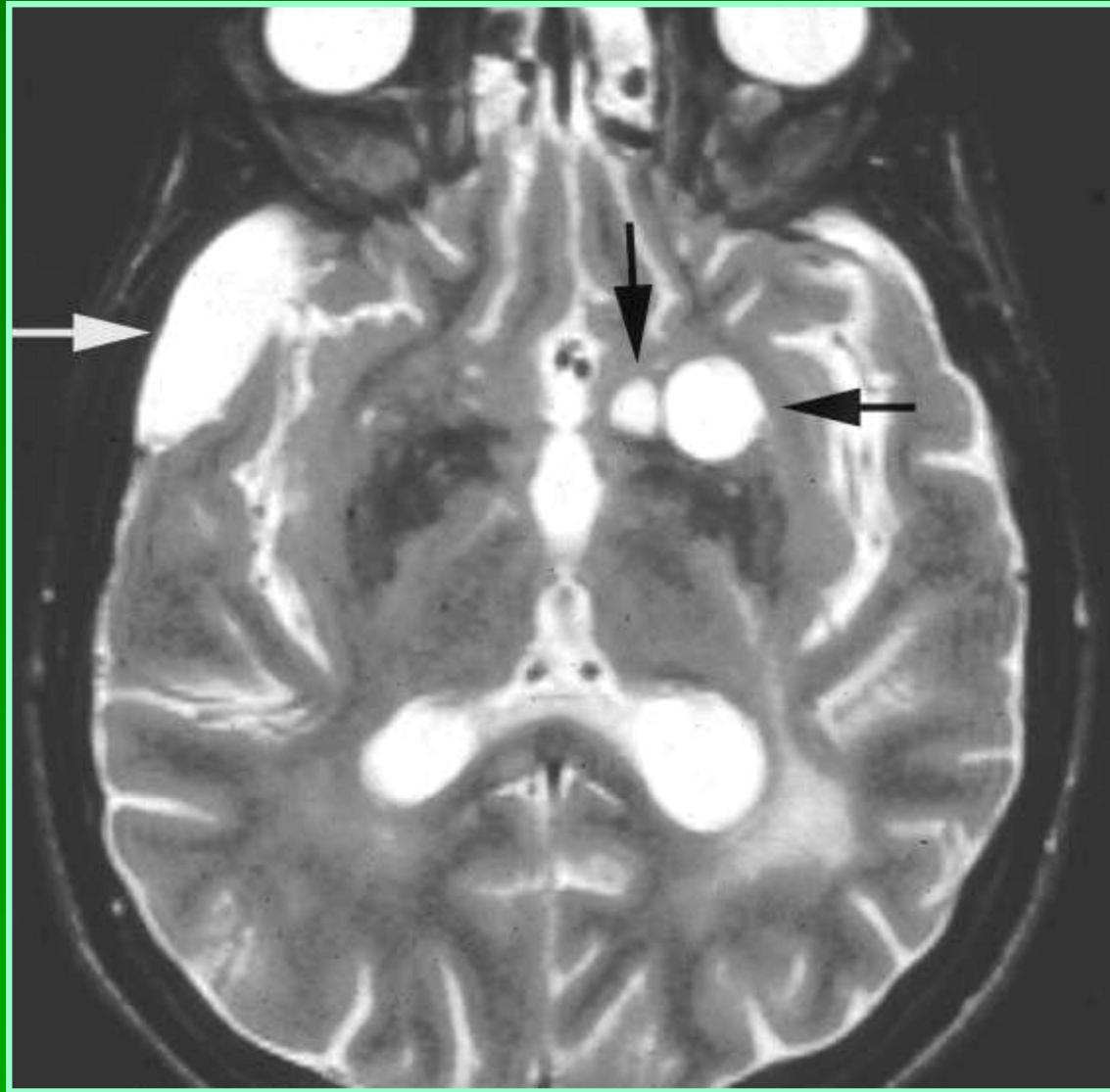
- *Altamente frecuente en nuestro medio*
- *CD 4+ < 100/ mm³*
- *Principal manifestación (frecuentemente la única) :
cefalea.*
- *Fiebre: 60 %*
- *H T I C (75 %) es la variable pronóstica determinante.*
- *Infiltrados pulmonares – 50 %*

CRYPTOCOCOSIS

Tipos diagnósticos:

- Hemocultivos (+) = 50 – 60 %
- P L normal N O ~~excluye~~ Dx (30 %)
- P L debe induir manometría (70 % > 200 mmH g)
- P L debe induir A g Crypto (Sensibil > 90 %)
- Tinta china = 60 – 80 %
- Sólo 40 % tendrán “M eningitis”
- Cultivos con volúmen de L CR 10 a 15 cc → 92 %

CRYPTOCOCOSIS



CRYPTOCOCOSIS



CRYPTOCOCOSIS

Aspectos relevantes en el manejo:

- Anfotericina B + FLU – 800 mg/d x 2 sem → → Fluconazol (800 x 8 Ss)
- El switch se basa en la respuesta clínica del paciente.
- 5-FC (100 mg/Kg/d) en lo posible, acelera esterilización del LCR.
- HTEC: Causa la mortalidad primeras 2 sem
 - PL evacuadora diaria si Pr. Aertura > 250 mmHg
 - Drenar 20 – 30 cc hasta PIC de cierre normal
 - Si persiste → Catéter peridural → DVP

CRYPTOCOCOSIS

Induction

The following is recommended as the preferred induction regimen:

- For adults, adolescents and children, a short-course (one-week) induction regimen with amphotericin B deoxycholate (1.0 mg/kg/day) and flucytosine (100 mg/kg/day, divided into four doses per day), followed by 1 week of fluconazole (1200 mg/day for adults, 12 mg/kg/day for children and adolescents, up to a maximum dose of 800mg daily), is the preferred option for treating cryptococcal meningitis among people living with HIV (*strong recommendation, moderate certainty evidence for adults, low-certainty evidence for children and adolescents*)

The following induction regimens are recommended as alternative options depending on drug availability:

- Two weeks of fluconazole (1200 mg daily for adults, 12 mg/kg/day for children and adolescents) + flucytosine (100 mg/kg/day, divided into four doses per day) (*strong recommendation, moderate-certainty evidence*).
- Two weeks of amphotericin B deoxycholate (1.0 mg/kg/day) + fluconazole (1200 mg daily for adults, 12 mg/kg/day for children and adolescents up to a maximum of 800 mg daily) (*strong recommendation, moderate-certainty evidence*).

CRYPTOCOCOSIS

Consolidation

Fluconazole (800 mg daily for adults, 6–12 mg/kg/day for children and adolescents up to a maximum of 800 mg daily) is recommended for the consolidation phase (for eight weeks following the induction phase) (*strong recommendation, low-certainty evidence*).

Maintenance (or secondary prophylaxis)

Fluconazole (200 mg daily for adults, 6 mg/kg/day for adolescents and children) is recommended for the maintenance phase (*strong recommendation, high-certainty evidence*).

Note: a minimum package of pre-emptive hydration and electrolyte replacement and toxicity monitoring and management should be provided to minimize treatment toxicity during induction phase with amphotericin B containing regimens and flucytosine.

***Diarrea
Compromiso G.I.***

- Bacterias
- Cryptosporidium
- Cistisospora
- Cyclospora
- Microsporidium
- Citomegalovirus
- Otras parasitosis

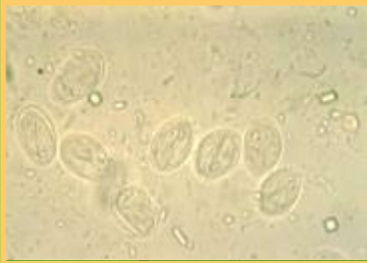
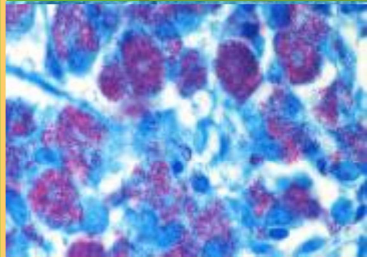
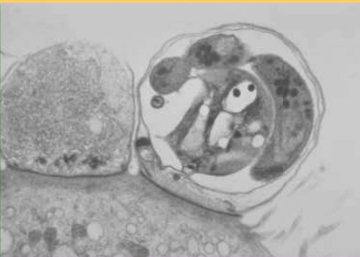
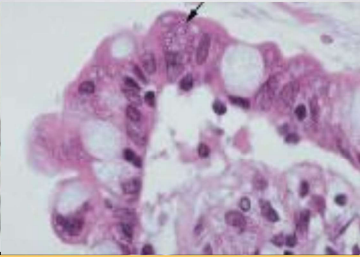
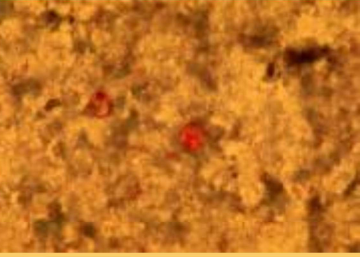
Ilustración	Sitio anatómico	Clínica	Dx	Patógeno / Tx
	I. Delgado y colon	Diarrea aguda, disentería, Fiebre	Cultivo MF Salmonella: Hemocultivo	<i>Salmonella, Shigella, C jejuni</i>
				Ciprofloxacina, Ceftriaxona
	I. Delgado, duodeno	Diarrea oleosa Aguda o Crónica	Visualización directa	<i>Giardia lamblia</i> Metronidazol Nitazoxanida Albendazol
	I. Delgado y colon, hígado, páncreas, ganglios	Diarrea crónica, Malabsorción, Anemia, leuco- penia	Cultivo MF Hemocultivo Cultivo MO	MAC Macrólido + ETB + Rifabutina/Cipro ± Amikacina
	Esófago, estómago, I. Delgado, colon, recto, retina, pulmón	Diarrea crónica Acuosa, hemorrágica	Colonoscopia + biopsia + Inmunohistoquímica	CMV Ganciclovir EV o valganciclovir oral

Ilustración	Sitio anatómico	Clínica	Dx	Patógeno / Tx
	I. Delgado	Diarrea acuosa, abundante, N & V, Dolor abdominal	Tinción BAAR 4 – 6 μ Biopsia Wright no inflam	<i>Cryptosporidium parvum</i>
				Nitazoxanida + HAART+Azitrom
	I. Delgado	Diarrea acuosa Aguda o Crónica Fiebre rara/.	Tinción BAAR 20 – 30 μ Wright neg.	<i>Cystoisospora belli</i> TMS-F 2 BID ó 1 TID Nitazoxanida
	I. Delgado	Diarrea acuosa, Sinusitis, cole- cistitis	Tinción tricromo Tinción BAAR 1 – 1.5 μ	<i>Microsporidiosis</i> (<i>E. Bieneusii</i> , <i>E. intestinalis</i>) Albendazol
	I. Delgado	Diarrea crónica acuosa	Tinción BAAR 8 – 10 μ Formas circulares	<i>Cyclospora cayetanensis</i> TMS-F QID

Sn Reconstitución inmune

Histoplasmosis

Cryptosporidiasis

Retinitis por CMV

***Con respecto de las
Otras . . .***

Sn Reconstitución inmune

Histoplasmosis

Cryptosporidiasis

Retinitis por CMV

*25 % pts en Tto ARV
Exacerbación inflamatoria
paradójica o puede
simula I.O. asociada*



Sn Reconstitución inmune

Histoplasmosis

Cryptosporidiasis

Retinitis por CMV



Sn Reconstitución inmune

Histoplasmosis

Cryptosporidiasis

Retinitis por CMV

Problema Dx:

- Baja sospecha
- Oportunidad del Ag
- Cultivos subóptimos

Problema terapéutico:

- Pobre pronóstico
- AnfoB liposomal → →
Itraconazol

Sn Reconstitución inmune

Histoplasmosis

Cryptosporidiasis

Retinitis por CMV



Sn Reconstitución inmune

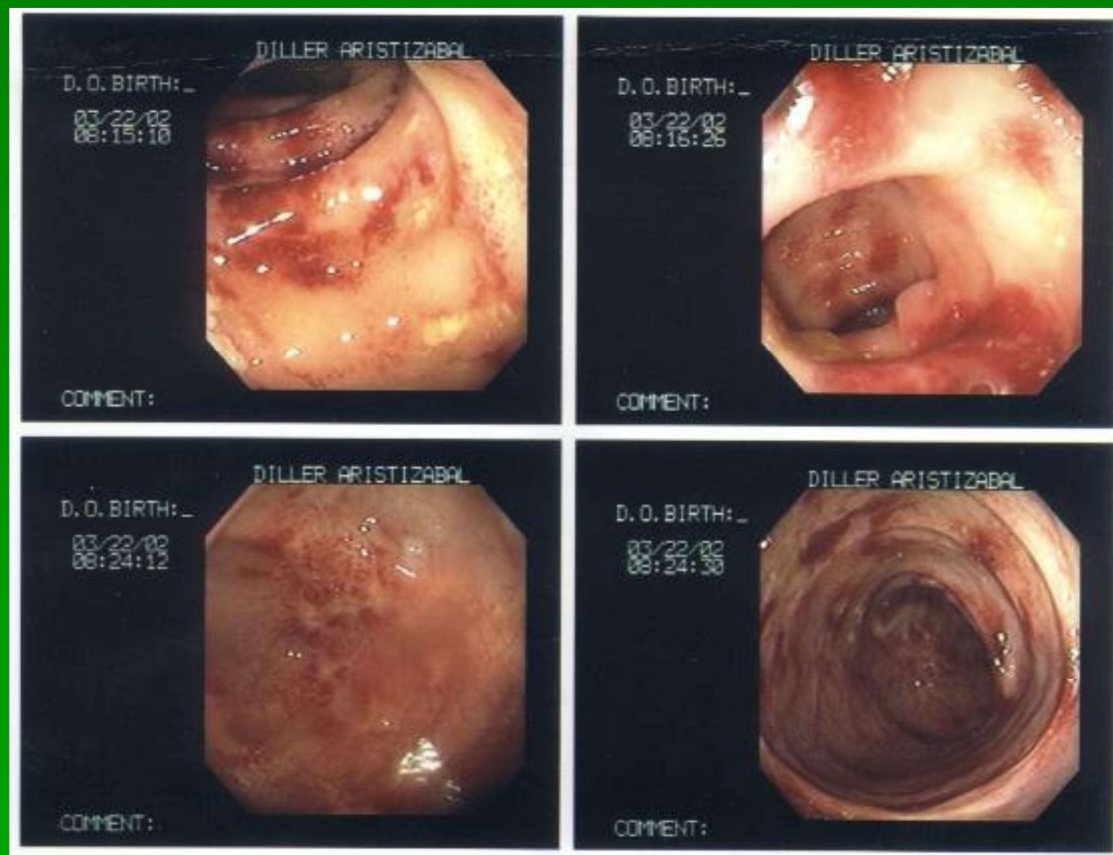
Histoplasmosis

Cryptosporidiasis

Retinitis por CMV

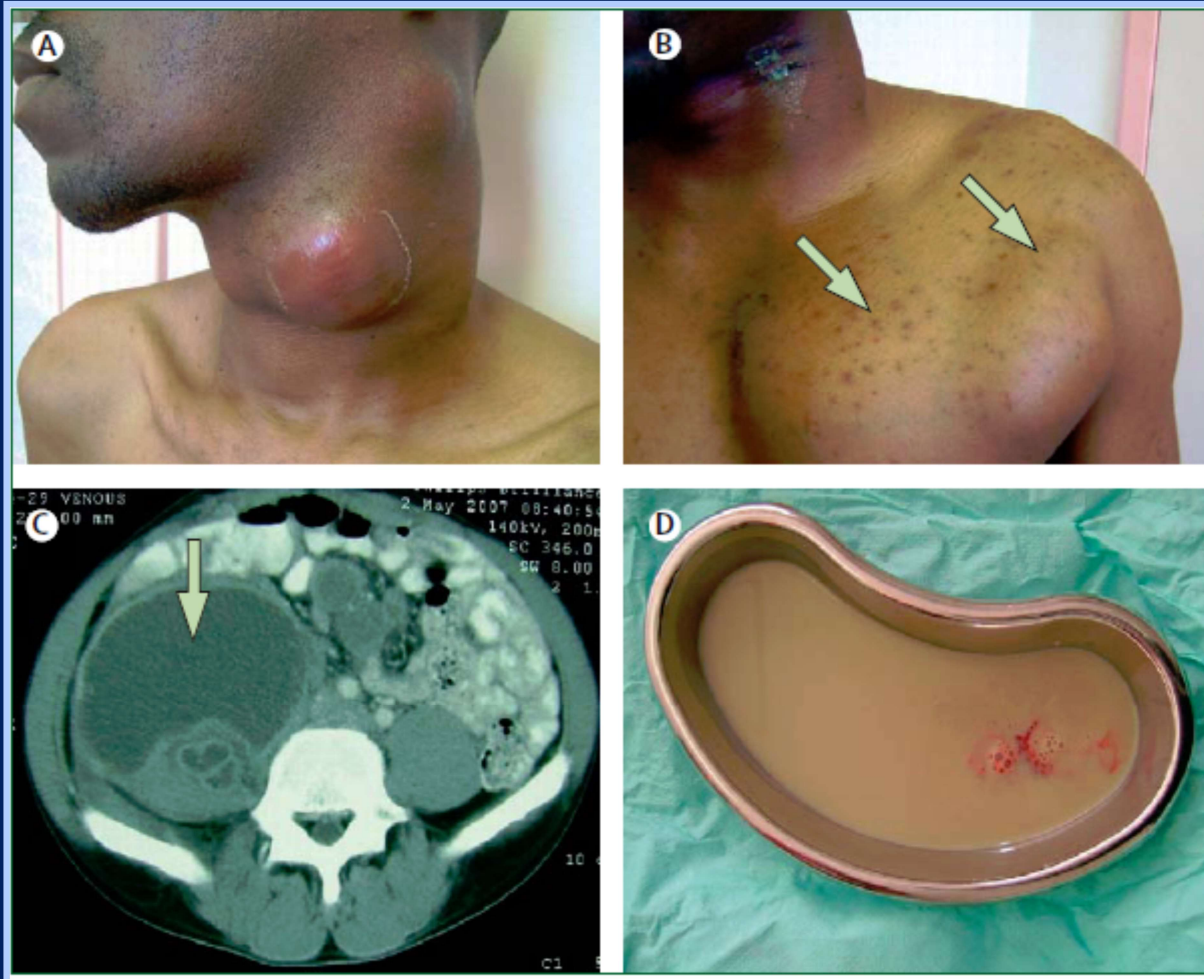
Grandes dramas:

- Sin pruebas confirm.
- Sin antivirales:
 - Cidofovir
 - Foscarnet
 - Formiversén
- Sin catéteres permanentes



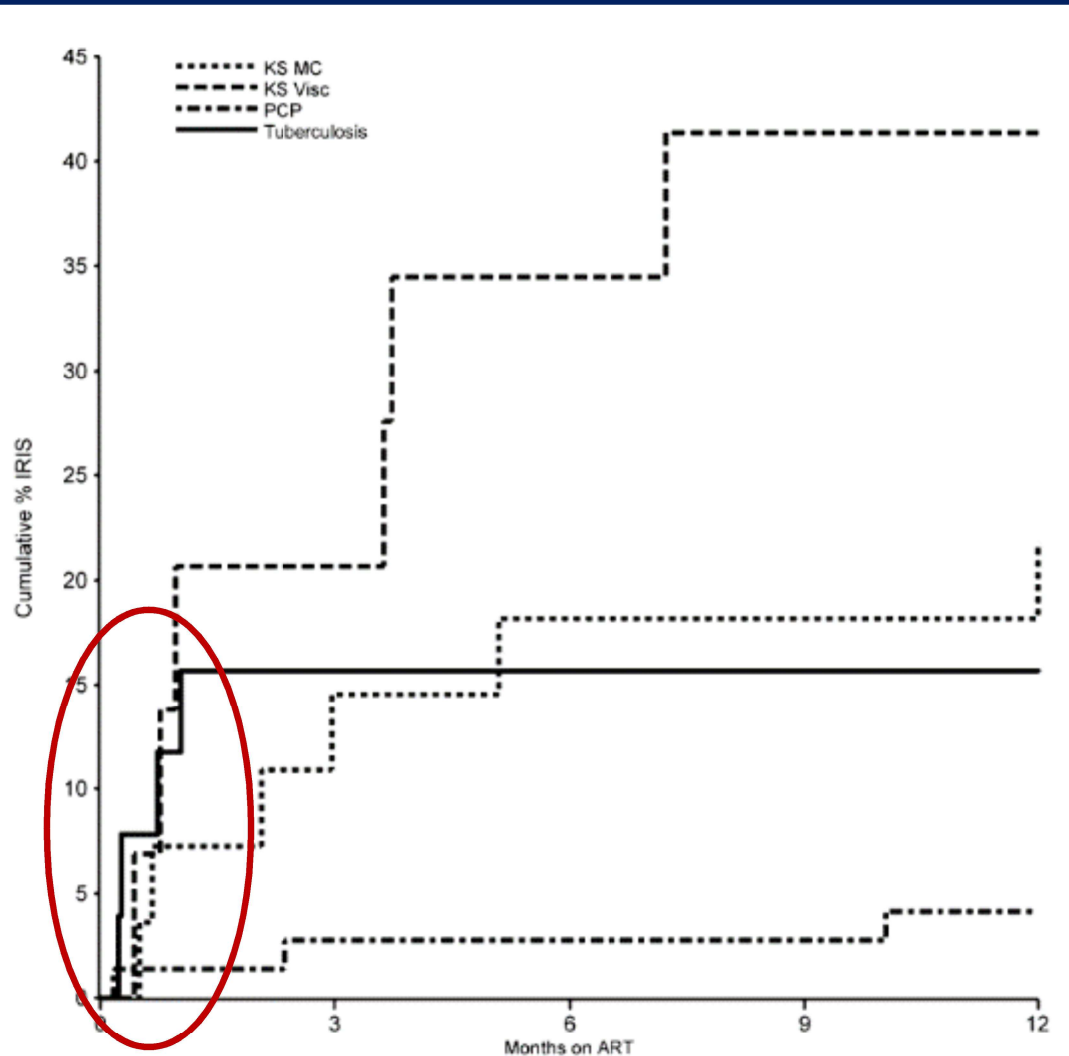
Compromiso extraocular por CMV (Colitis)

IRIS (*Immune reconstitución inflammatory syndrome*)



Presentaciones atípicos de tuberculosis

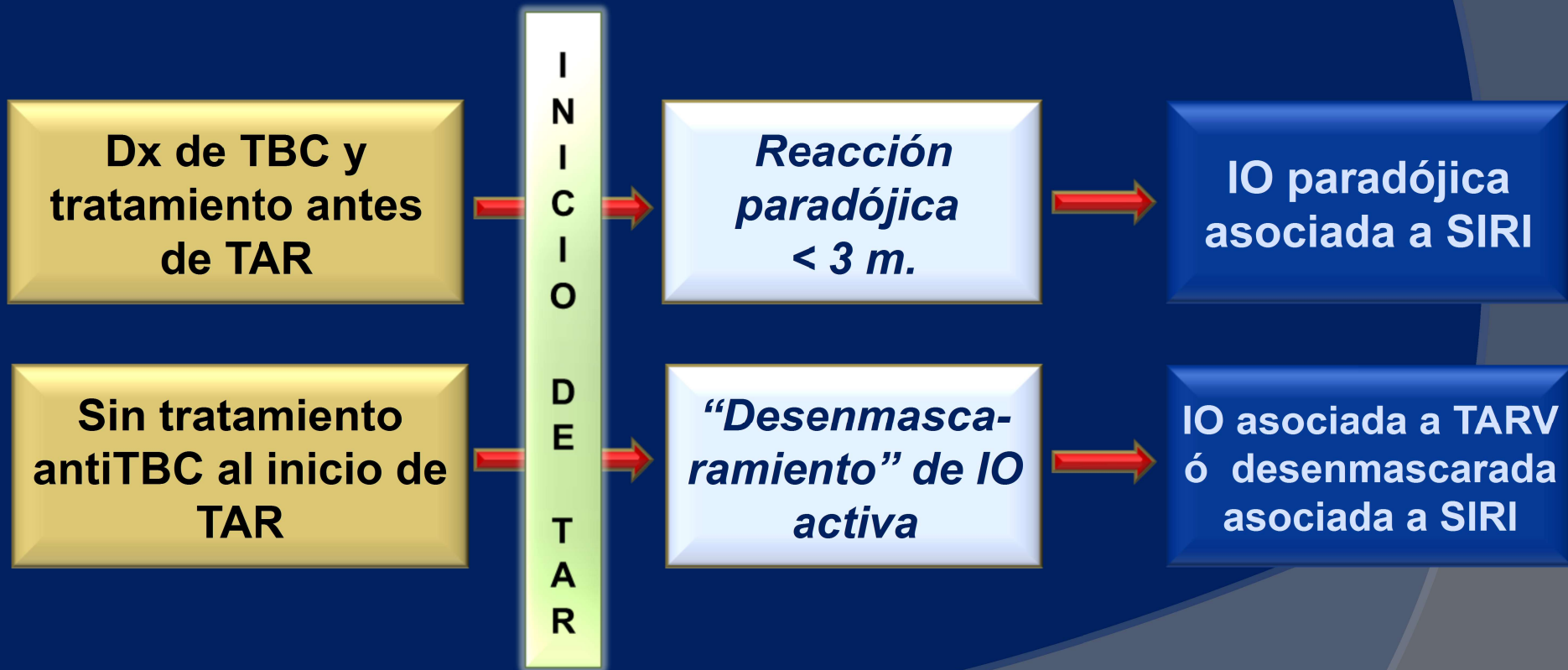
IRIS paradójico en pacientes con VIH iniciados en TARV después de infección oportunista trazadora de SIDA



- 196 pacientes con 260 IOs,
- Incidencia acumulada a 1 año:
 - 29% (12/41) → KS,
 - 16% (4/25) → tuberculosis,
 - 14% (1/7) → Cryptococcus,
 - 10% (1/10) → MAC,
 - 4% (3/72) → PCP.

IRIS (*Immune reconstitución inflammatory syndrome*)

Tuberculosis asociada a SIRC: Definición de caso para países con recursos limitados



Alta mortalidad temprana en pacientes bajo TARV

(N = 559 pts sin tto previo 3 años de TARV en Uganda)

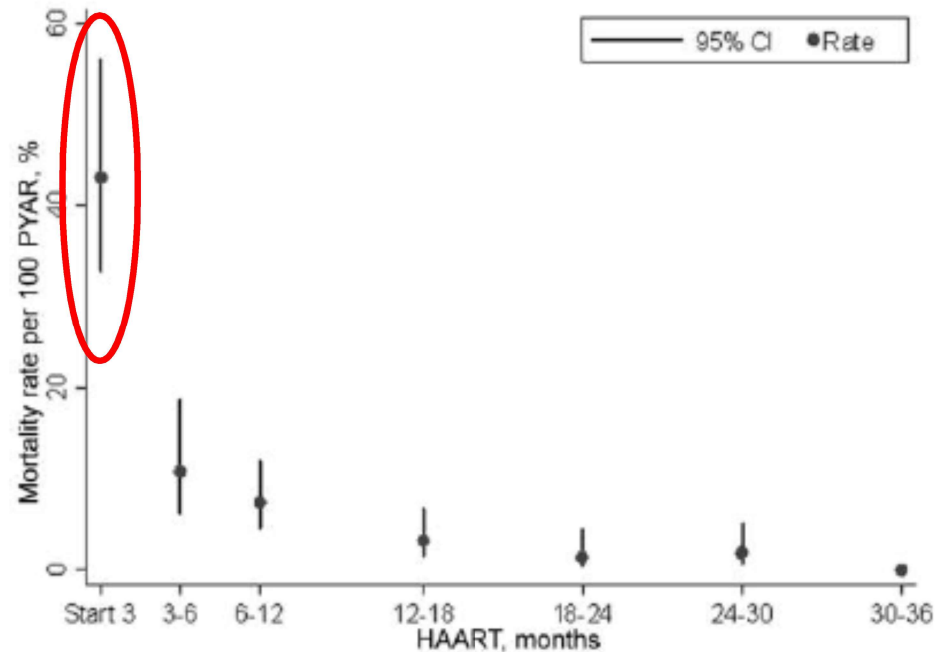
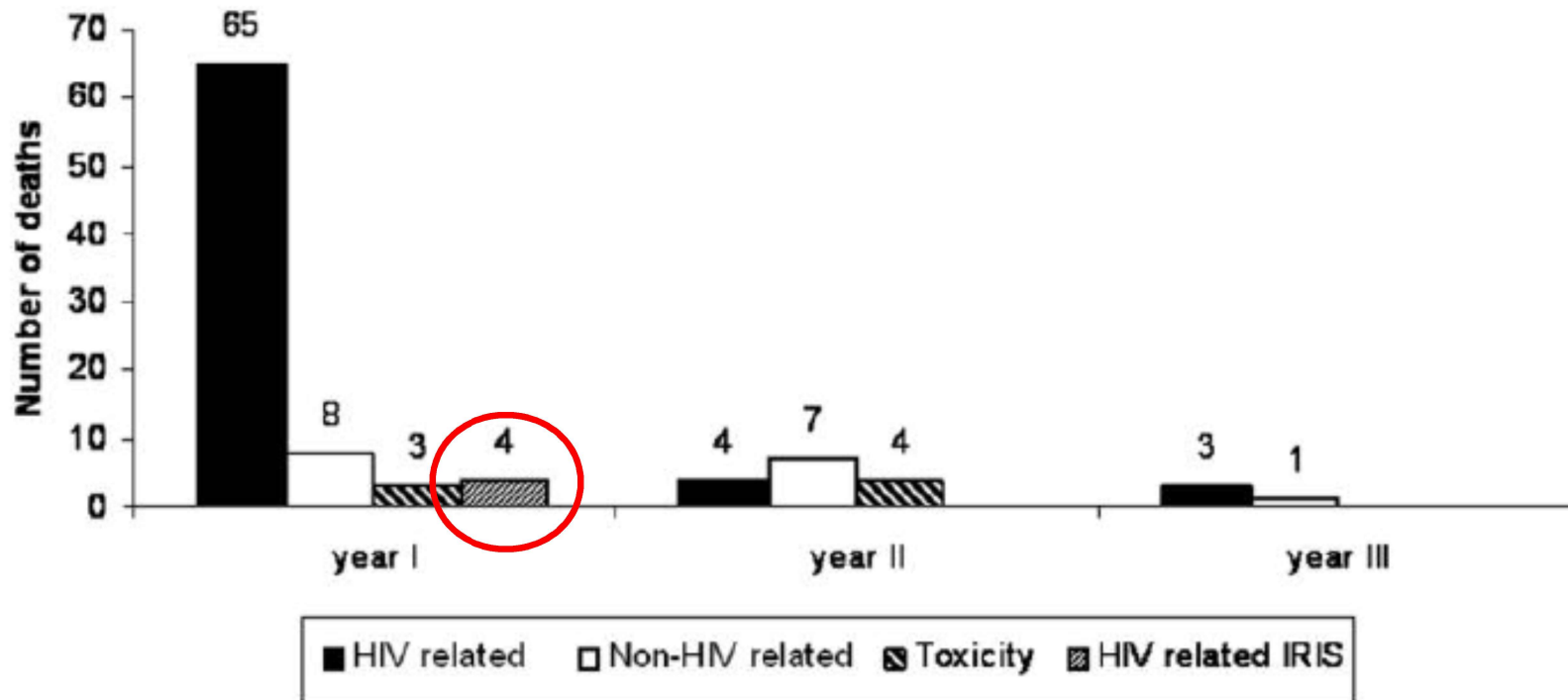


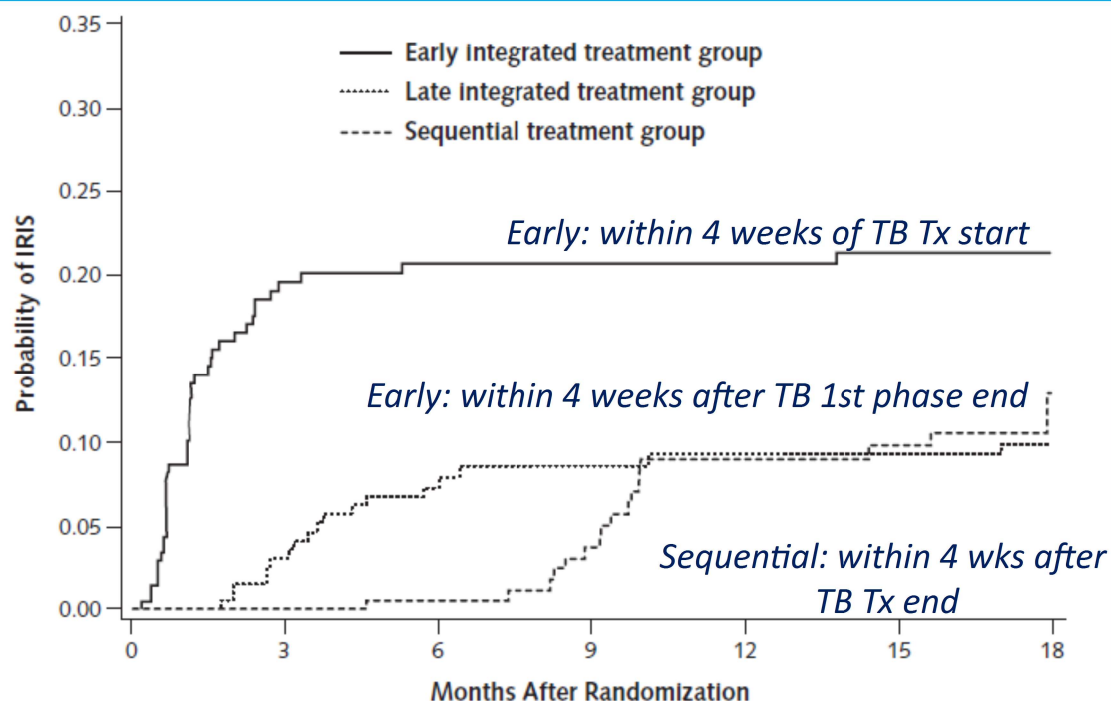
Figure 1. All-cause mortality incidence rates (95% confidence interval [CI]) during the first 36 months of antiretroviral treatment, showing highest rates per 100 person-years at risk (PYAR) during the first 3 months after highly active antiretroviral therapy (HAART) initiation.

IRIS: Baja mortalidad

(N = 559 pts sin tto previo 3 años de TARV en Uganda)



IRIS en pacientes con TBC: Estudio SAPiT



IRIS Events/Patients in Follow-up (Deaths; Withdrawals)

Early Integrated treatment	214	40/156 (4; 14)	42/145 (7; 20)	42/141 (8; 23)	42/138 (9; 25)	43/131 (9; 31)	43/121 (12; 38)
Late Integrated treatment	215	6/188 (1; 20)	14/167 (5; 29)	16/153 (9; 37)	17/143 (11; 44)	17/139 (12; 47)	18/128 (14; 55)
Sequential treatment	213	0/196 (3; 14)	1/179 (12; 21)	6/152 (20; 35)	14/130 (31; 38)	15/121 (32; 45)	19/110 (33; 51)

IRIS en pacientes con TBC: Estudio SAPIt

Table 3. IRIS Severity, by Study Group

Variable	Early Integrated Treatment Group	Late Integrated Treatment Group	Sequential Treatment Group
Patients with IRIS, <i>n</i>	43	18	19
Grade 3 or 4 IRIS, <i>n</i> (%) [*]	15 (35)	4 (22)	3 (16)
Hospitalization for IRIS, <i>n</i> (%)	18 (42)	4 (22)	1 (5)
Received steroids for IRIS, <i>n</i> (%)	4 (9)	1 (6)	3 (16)
Complete resolution of IRIS without sequelae, <i>n</i> (%)	38 (88)	18 (100)	16 (84)
Median time to IRIS resolution (IQR), <i>d</i>	70.5 (42 to 151)	34.0 (24 to 118)	23.5 (11.5 to 40.5)
IRIS-associated deaths, <i>n</i> (%)	2 (5)	0	0
Median time to IRIS from ART initiation (IQR), <i>d</i>	17.5 (10 to 30)	17 (14 to 28)	28 (14 to 44)
Median CD4 ⁺ count (IQR), $\times 10^9$ cells/L	0.101 (0.036 to 0.172)	0.117 (0.045 to 0.342)	0.132 (0.033 to 0.251)

Uso de prednisona en pacientes VIH+ con SRI asociado a TBC

Estudio doble ciego aleatorizado controlado con placebo

- n = 109, Prednisona: 55, plac: 54. 64% – Mujeres. Mediana edad: 32 a.
- Prednisona = 1.5 mg/kg/day (2 sem) luego 0.75 mg/kg/day (2 sem). Seguimiento por 12 sem.
- CD4+ antes de TARV = 53 céls/ μ L, al ingreso al estudio = 116
- Mediana - días de hospitalización: 1 vs 3 (p = 0.05).
- Muertes: 3 vs 2 (p = 0.7).
- Efectos colaterales de esteroides: 9 vs 3 ptes (p = 0.07).
- Infecciones severas: 2 vs 4 (p = 0.4).
- Mejoría en puntaje de 5 puntos sobre síntomas a 2 sem (p = 0.003).

Prednisone for the Prevention of Paradoxical Tuberculosis-Associated IRIS

(40 mg/d x 2 wks, then 20 mg/d x 2 wks or placebo)

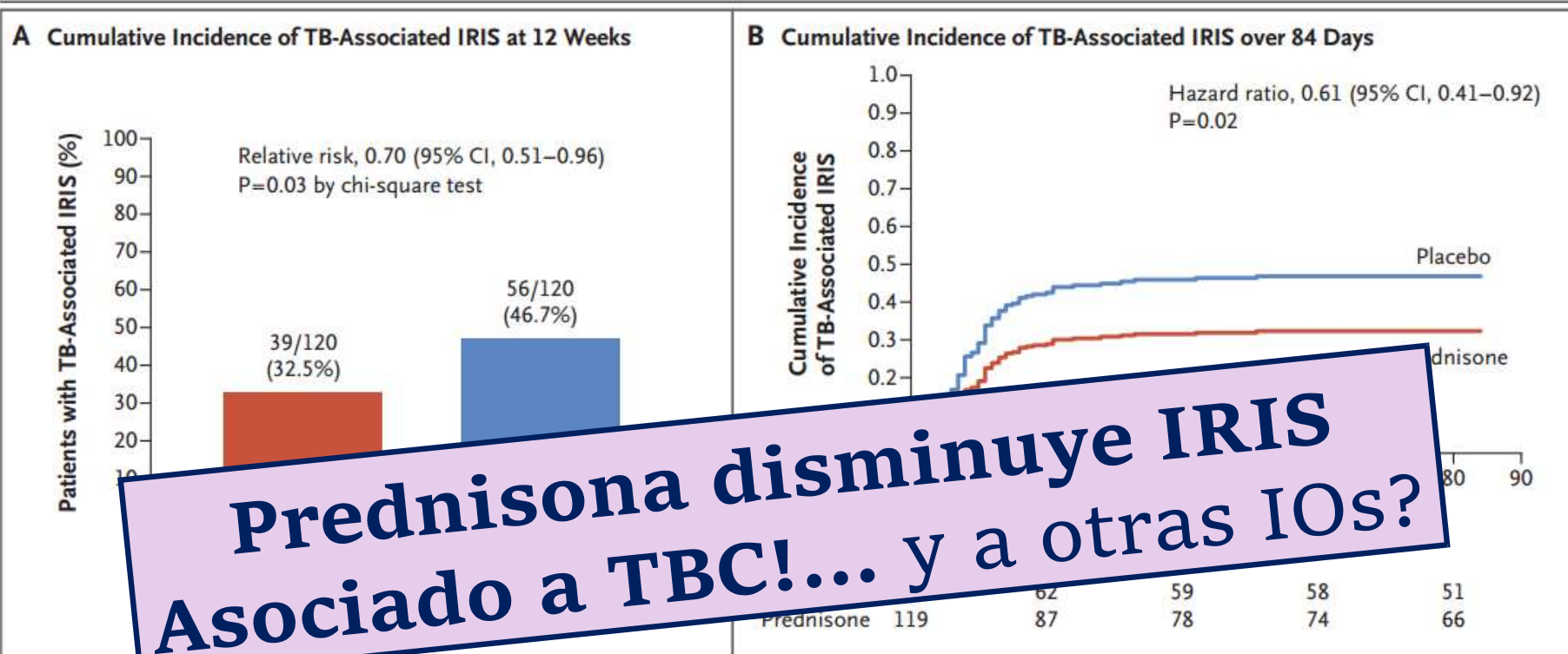


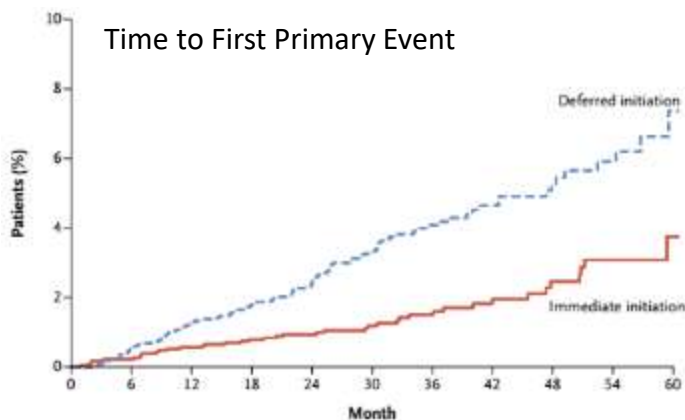
Figure 2. Cumulative Incidence of Paradoxical TB-Associated Immune Reconstitution Inflammatory Syndrome (IRIS).

Panel A shows the cumulative incidence of the primary end point of paradoxical TB-associated IRIS at 12 weeks. If paradoxical TB-associated IRIS had not developed before a patient died, withdrew, or was lost to follow-up, the patient was considered not to have had the syndrome. Panel B shows the cumulative incidence of TB-associated IRIS over 84 days. Diagnosis of TB-associated IRIS was determined according to the International Network for the Study of HIV-associated IRIS criteria.¹⁴ Day 0 is the day ART was initiated.

Estudios INSIGHT START y TEMPRANO: Cambiaron la historia de la T.A.R.

Inicio pronto y rápido de TAR

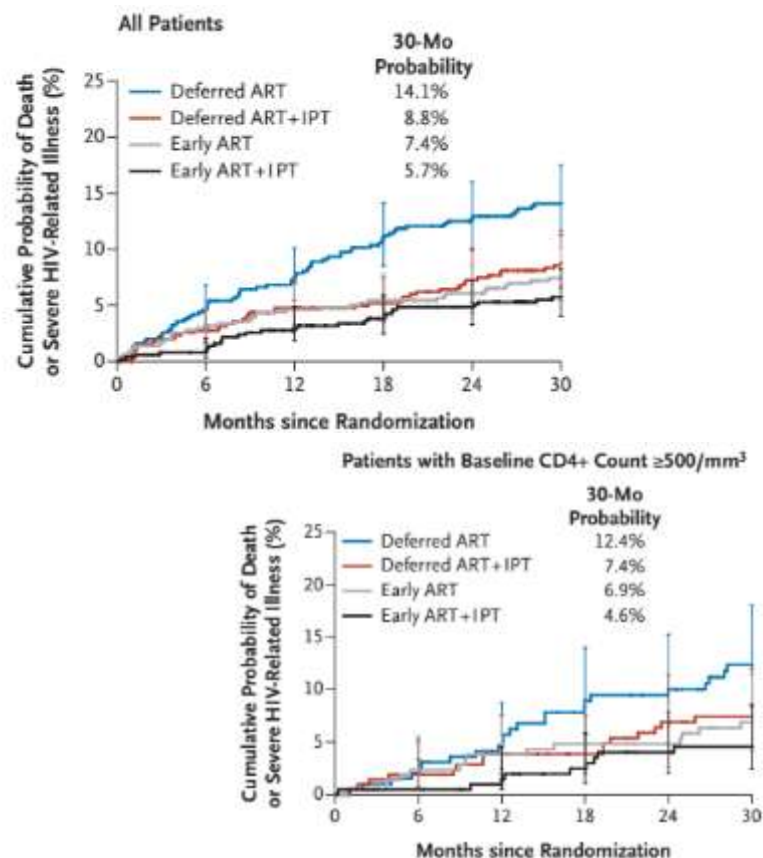
INSIGHT
START



Latest CD4+ count > 500 cells/mm³

	Immediate ART	Deferred ART
Primary events, % (n/N)	88 (37/42)	59 (57/96)
Rate/100 PY	0.6	1.1

TEMPRANO



The INSIGHT START Study Group. N Engl J Med 2015; 373:795-807

The TEMPRANO Study Group. N Engl J Med 2015; 373:808-822

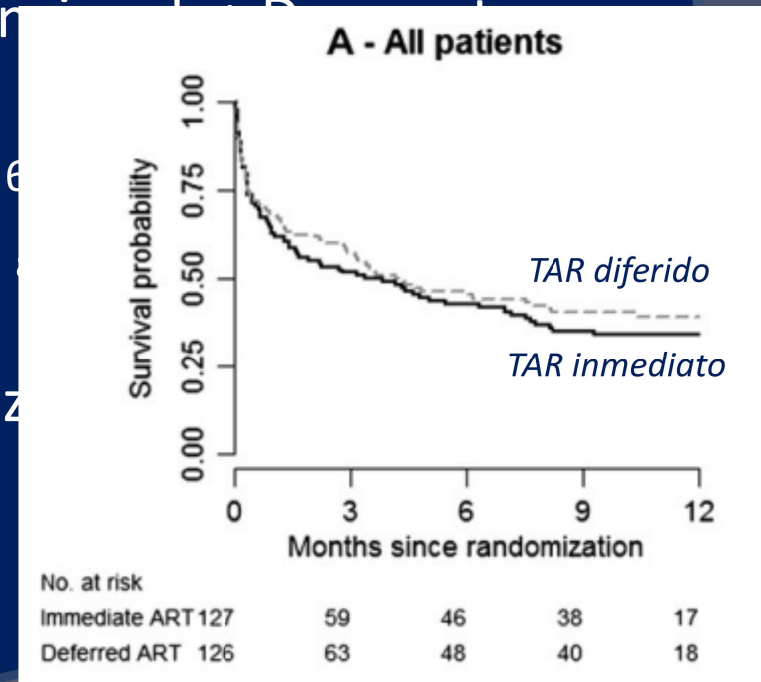
Tuberculosis associated immune reconstitution inflammatory syndrome in patients infected with HIV: meningitis a potentially life threatening manifestation

Upasna Agarwal^{1*}, Amitabh Kumar¹, Digamber Behera¹, Martyn A French² and Patricia Price²

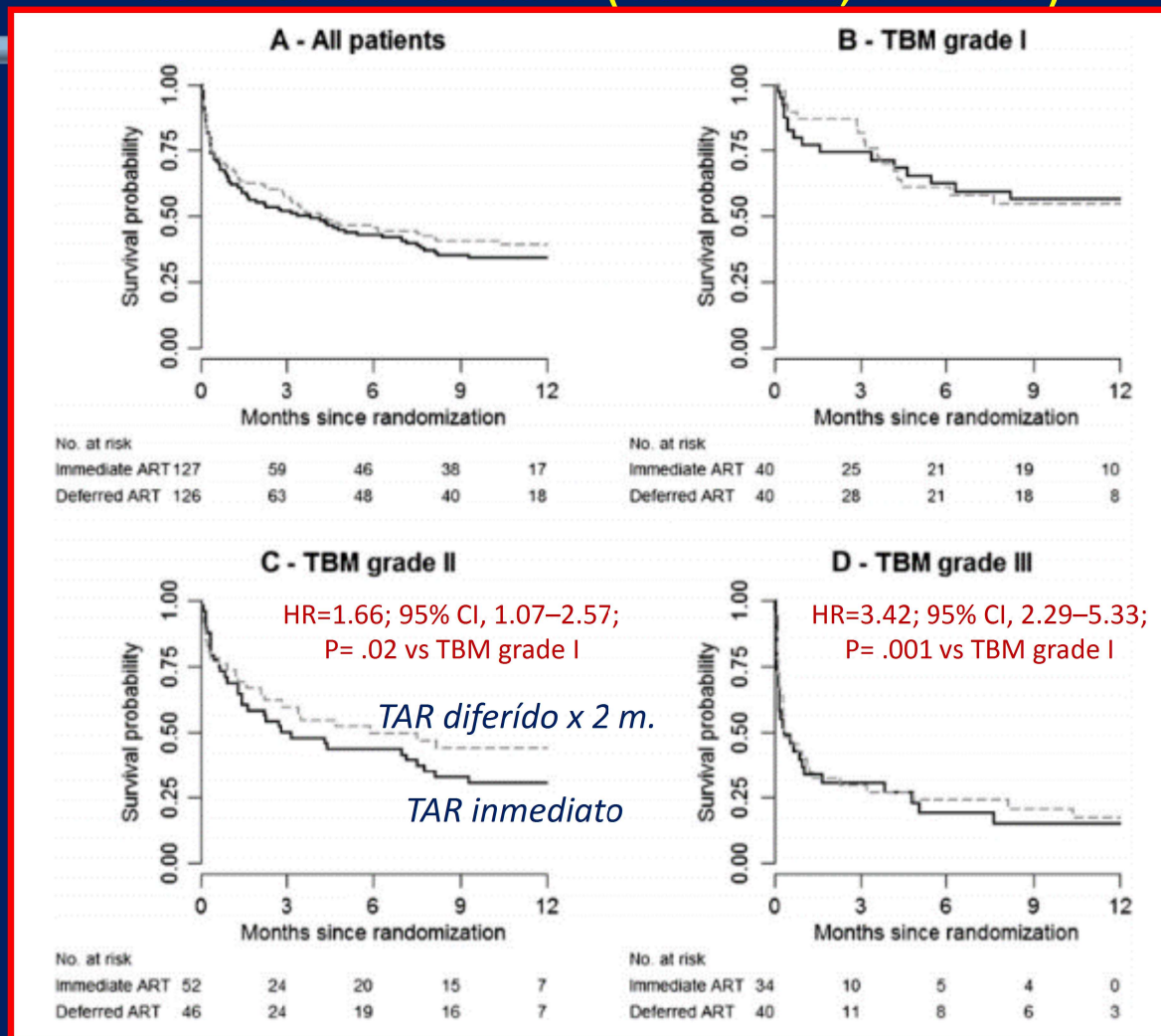
- 514 pacientes
- 13 (12.6%) desarrollaron IRIS asociada a TBC
- Presentaciones: 11 / 15 con IRIS leve o moderado.
 - Linfadenopatías nuevas (n = 3),
 - Aumento de tamaño de linfadenopatías existentes (n = 3),
 - Deterioro de lesiones pulmonares (n = 2),
 - Nuevo derrame pleuras (n = 1)
 - Fiebre alta prolongada (n = 2).
- **Cuatro pacientes → Meningitis TBC asociada a IRIS**
(mediana de 15 días de inicio de TARV), > 35 años (P = 0.03), sin diferencias en CD4, duración de tto antiTBC previo al inicio de TARV o el resultado de la TBC.
- **8 (62%) pacientes → Recuperación completa**
- **5 (38%) con TB-IRIS murieron, 3 de los cuáles tenían meningitis.**

Tiempo de inicio de TARV en meningitis TBC asociada a VIH

- 253 pacientes aleatorizados:
- 127 – Brazo de inicio de TARV inmediato (con tto antiTBC)
- 126 – Brazo con TARV diferido (2 meses después)
- Tto antiTBC – tetraconjugado convencional con Rifampina y Pirazinamida IV.
- TARV: AZT + 3TC + EFV (800 mg con RIF, 600 mg con PZA)
- Murieron 76 y 70 pacientes en cada brazo durante el seguimiento.
- Mayor tasa de EAs grado 4 en el brazo con TARV diferido
 - 61 vs 47 pctes ($p = 0.03$)



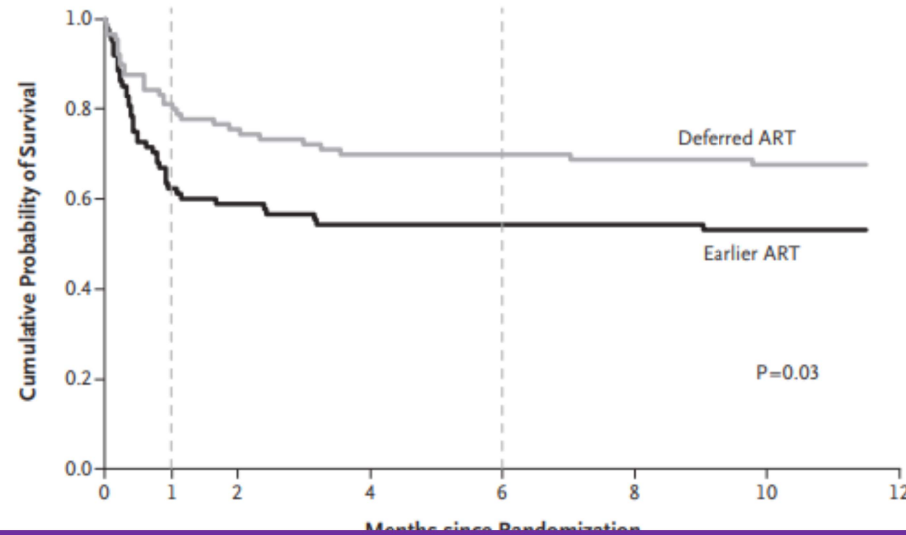
Tiempo de inicio de TARV en meningitis TBC asociada a VIH (Vietnam, n= 253)



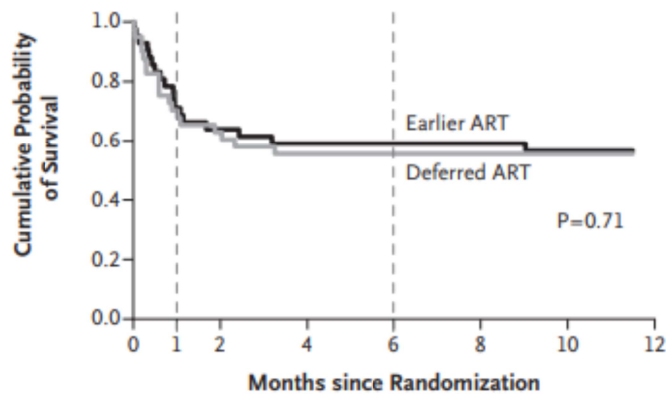
Baseline TBM disease grade was a strong independent predictor for death (HR for TBM grade II, 1.66; 95% CI, 1.07–2.57; P= .02 compared with TBM grade I; HR for TBM grade III, 3.42; 95% CI, 2.29–5.33; P = .001 compared with TBM grade I)

Inicio de TAR en meningitis por criptococo: El estudio COAT (Uganda, n= 177)

A Overall Survival



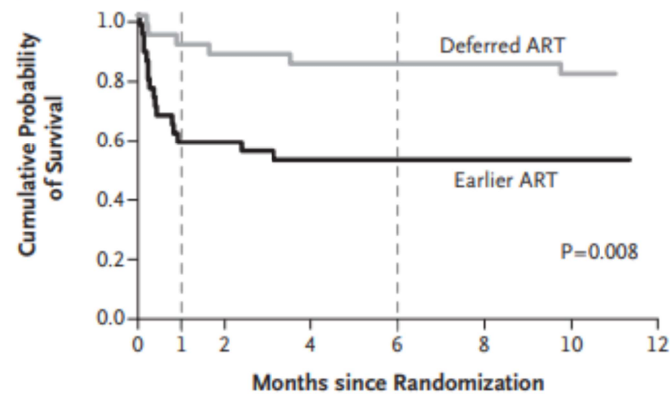
B Survival in Those with CSF White-Cell Count ≥ 5 Cells per mm^3 at Randomization



No. at Risk

Earlier ART	42	29	26	24	24	23	21
Deferred ART	40	28	25	22	22	22	22

C Survival in Those with CSF White-Cell Count < 5 Cells per mm^3 at Randomization



No. at Risk

Earlier ART	33	19	19	17	17	17	16
Deferred ART	31	28	27	26	26	26	24

Integrase Inhibitors are an Risk Factor for IRIS: an ATHENA-Cohort Study

Incidences of both forms of IRIS:

	INI (N=69)	n-INI (N=300)	Total (N=369)
Type IRIS			
IRIS _{FRENCH} , N(%)	13 (19)	27 (9)	40 (11)
IRIS _{CLINICAL} , N(%)	13 (19)	20 (7)	33 (9)
Total, N (%)	26 (38)	47 (16)	73 (20)

OR IRIS_{FRENCH}: 2.35 (95% CI 1.14 – 4.83)

OR IRIS_{CLINICAL}: 3.25 (95% CI 1.53 – 6.91)

OR IRIS_{TOTAL}: 3.25 (95% CI 1.83 – 5.80)

Cox regression analysis:

	IRIS _{FRENCH+CLINICAL} HR (95% CI), p-value	IRIS _{FRENCH} HR (95% CI), p-value
Use of INI	2.69 (1.63-4.44), 0.0001	2.62 (1.35-5.10), 0.0045
Female gender	1.64 (0.97-2.78), 0.067	-
Diagnosed with CM	3.71 (1.55-8.88), 0.0033	11.6 (4.77-28.3), <0.0001
Diagnosed with MAC	2.46 (1.04-5.84), 0.041	-
Diagnosed with CMV	2.25 (1.06-4.79), 0.035	4.23 (1.84-9.74), 0.0007

INI = integrase Inhibitor, CM = Cryptococcal Meningitis, MAC = Mycobacterium Avium Complex, CMV = CytoMegalovirus.

Initiation of ART based on Integrase Inhibitors increases the risk of IRIS

Characteristics at ART initiation and evolution compared between patients receiving INSTI (INSTI+) and patients not receiving INSTI (INSTI-).

		ART with INSTI N=398	ART without INSTI N=1889	p
IRIS Cases, N(%)		12 (3.0)	29 (1.5)	0.05
OR [95% CI]		1.99 [1.09-3.47]	Ref.	0.04
IRIS related to	M. tuberculosis	5 (42%)	7 (58%)	0.81
	M. avium	2 (20%)	8 (80%)	
	Progressive Multifocal Leukoencephalopathy	1 (16.7%)	5 (83.3%)	
	CMV	2 (40%)	3 (60%)	
	Kaposi sarcoma	2 (50%)	2 (50%)	
	C. neoformans	0	1	
	Toxoplasmosis	0	2	
	Hepatitis B	0	1	

Efficacy And Safety Of Dolutegravir-based Regimens In Advanced HIV/AIDS, Italy.

Figure 1. AIDS-defining events according to ART-regimens
(n= 178 in 120 patients)

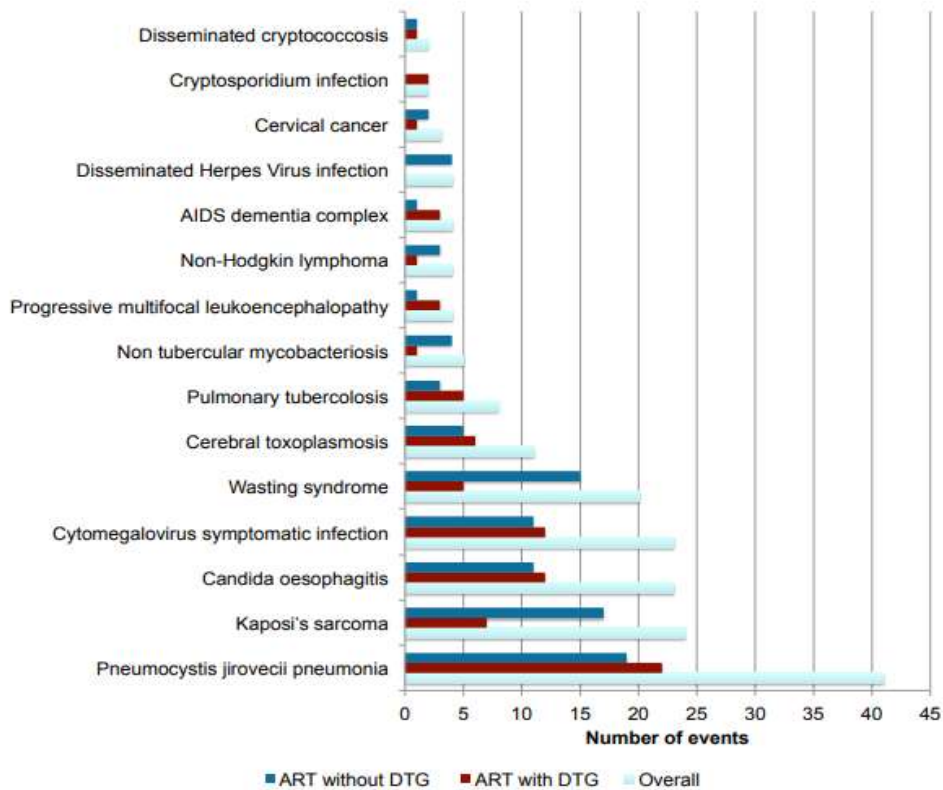
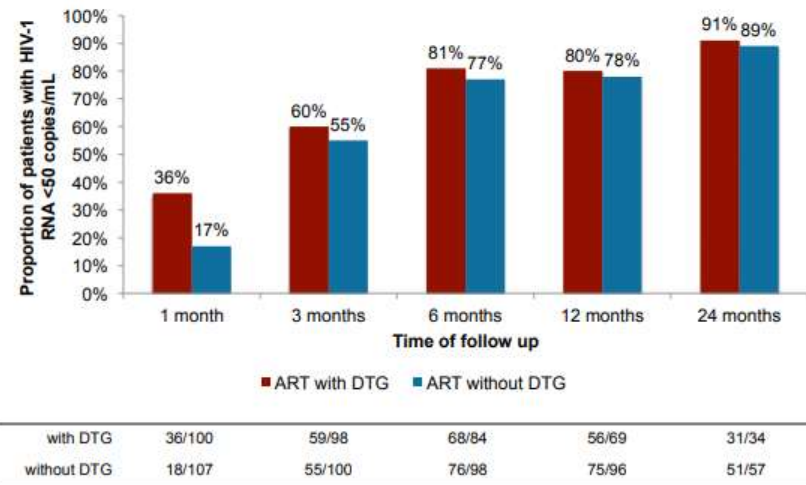


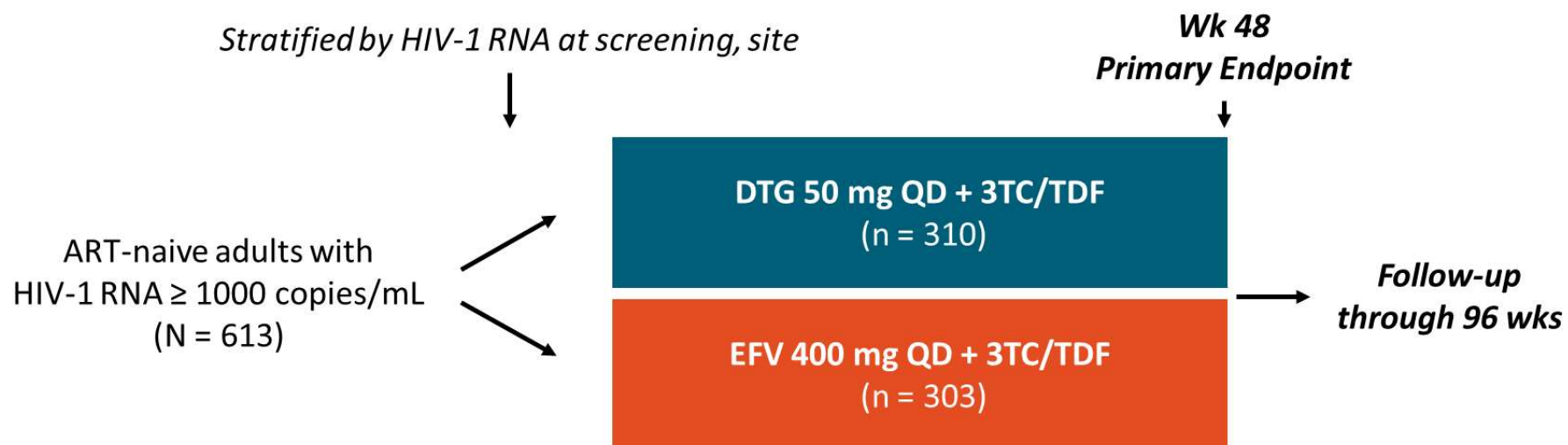
Figure 3. HIV-1 RNA<50 cps/mL had been achieved in 95/132 (72%) patients on ART with DTG and in 92/140 (66%) patients on ART without DTG



- Multicenter retrospective cohort, Italy.
- IRIS was reported in 13/272 (5%) AIDS-presenters:
 - 5/132 (4%) among patients on DTG-based regimens
 - 8/140 (6%) among those without DTG-based regimens

NAMSAL: DTG- vs EFV 400 mg in Treatment-Naive Patients in Cameroon

- Multicenter, randomized, open-label phase III noninferiority trial



- Primary endpoint: HIV-1 RNA < 50 copies/mL at Wk 48 (FDA Snapshot)
 - Noninferiority tested with 10% margin



Slide credit: clinicaloptions.com

NAMSAL: Efficacy at Wk 48 (FDA Snapshot)

Outcome at Wk 48	DTG + 3TC/TDF (n = 310)	EFV 400 + 3TC/TDF (n = 303)	Treatment Difference DTG - EFV (95% CI), %
HIV-1 RNA < 50 c/mL (virologic success), n (%)	231 (74.5)	209 (69.0)	5.5 (-1.6 to 12.7)
HIV-1 RNA < 200 c/mL/< 1000 c/mL, %	89.0/91.9	83.5/86.5	--
HIV-1 RNA > 50 c/mL (virologic failure), n	62	70	--
▪ D/c for death	6	7	--
▪ D/c other reasons (LTFU, withdrawn)	9		--
HIV-1 RNA < 50 c/mL by BL VL, n/N (%)			
▪ HIV-1 RNA < 100,000 c/mL			7.8 (-1.2 to 16.8)
▪ HIV-1 RNA < 1000 c/mL		123/200 (61.5)	4.7 (-4.6 to 14.0)
▪ HIV-1 RNA > 1000 c/mL	51/93 (54.8)	55/95 (57.9)	--

Y los resultados del SINGLE?

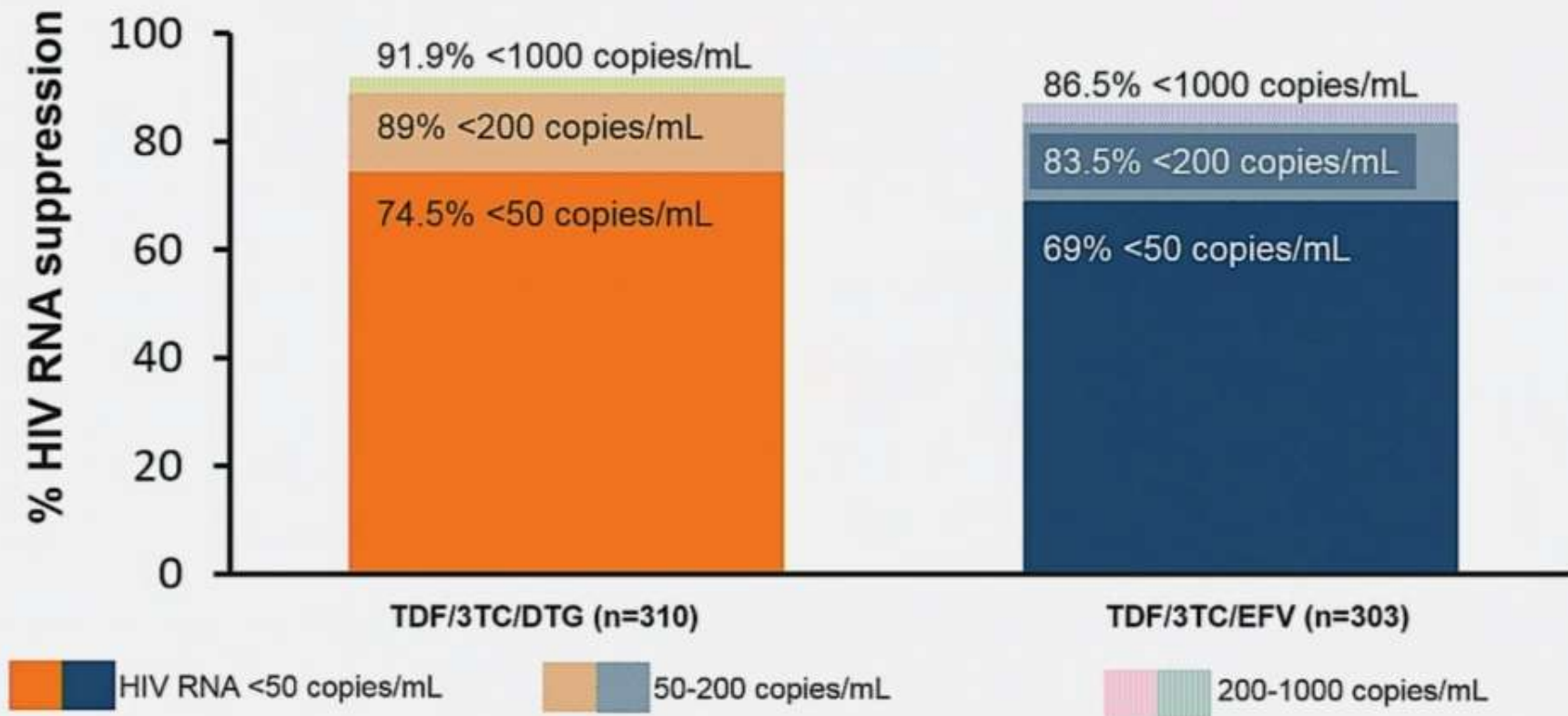
- AEs: DTG 11% vs EFV 400 8%; AIDS-defining events: DTG 8% vs EFV 400 10%
- **Virologic failure (HIV-1 RNA > 1000 c/mL) observed in 19 pts; emergent resistance in 0/3 DTG failures vs 9/16 EFV 400 failures**



Slide credit: clinicaloptions.com

DTG vs EFV-400mg for initial treatment in Cameroon- 48wk results, NAMSAL Trial

HIV RNA suppression at Week 48 (ITT)



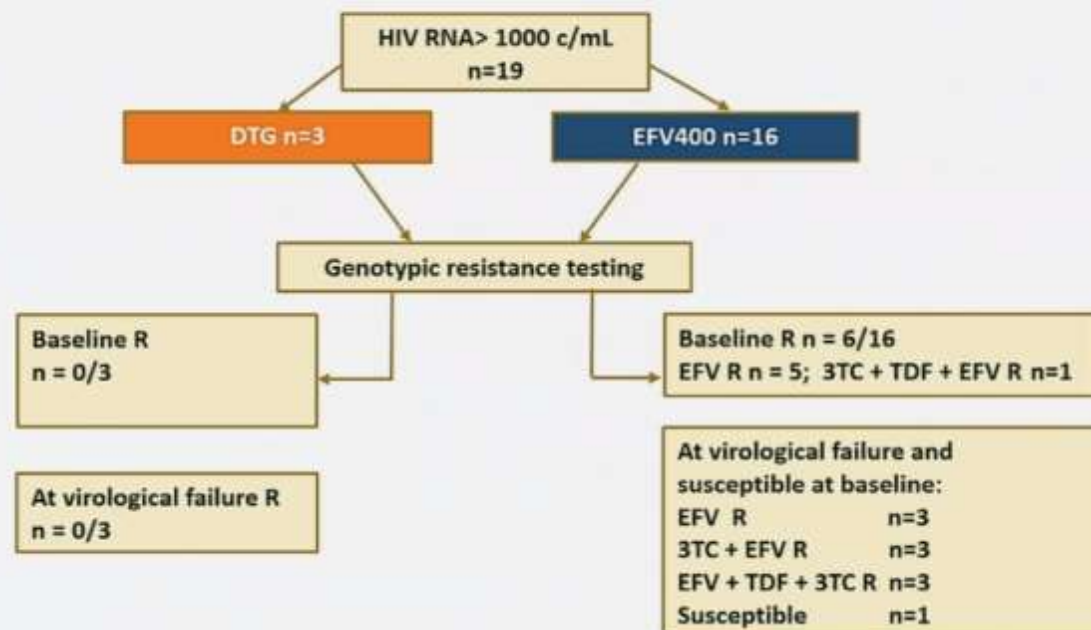
DTG vs EFV-400mg for initial treatment in Cameroon- 48wk results, NAMSAL Trial

Secondary outcomes

	TDF/3TC + DTG (N=310)	TDF/3TC + EFV400 (N=303)	TOTAL (N=616)
Adverse Events n (%)	34 (11%)		
AIDS Defining Events n(%)	25 (8%)	2	

No treatment interruptions due

Virological failure > 1000copies/mL (WHO) and resistance



En resumen . . .

- El VIH es y seguirá siendo una causa frecuente de consulta en nuestros servicios de urgencias.
- ... tanto por infecciones oportunistas como por causas no relacionadas a SIDA
- El enfoque, en lo posible, debe ser hacia establecer diagnóstico, no empirico.
- IRIS es frecuente, pero no severo, no resulta en mortalidad
- No iniciar TAR pronto, sí resulta en mayor mortalidad
- ... excepto en meningitis por criptococo y por tuberculosis
- TAR idealmente basada en INSTIs, pero EFV ok si no hay contraindicaciones

Muchas gracias