Experiencias exitosas en Investigacion Clinica: El caso de Fundacion Huesped

Pedro Cahn

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Para ser investigador hay que ser…

Curioso!

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Motivaciones para investigar

- Curiosidad
- Interés en mejorar la vida de los pacientes
- Discomfort con la realidad
- Interés intelectual
- Ego, Interés en sobresalir
- Razones personales

Principios de la investigación

Que se necesita para un buen centro

Investigador líder

Idea

Recursos

Equipo

Infraestructura

Acceso a voluntarios

Acceso a poblaciones afectadas:
Colaboracion FH-ATTA

MOST AFFECTED KEY POPULATION

- *Extremely lower life expectancy (estimed **35 years**)*
- *Impressive discrimination, isolation and lack of support*
- *High prevalence of infections*
  - *HIV prevalence: 34%*
  - *HCV: 4.5%*
  - *Syphilis: 50,4%*
  - *HPV: 97%*

ASOCIACION TRAVESTIS TRANSEXUALES TRANSGENEROS ARGENTINA CHUBUT

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Proyectos

TransTesting

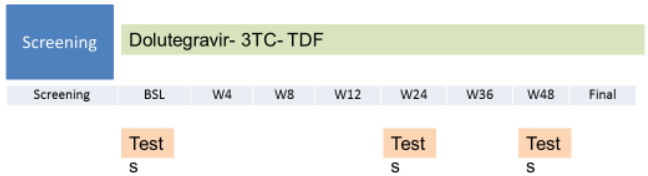
- 200 TGW will be tested simultaneously via the 3 tests to determine:
  - Sensitivity
  - Specificity
  - Positive predictive value (PPV)
  - Negative predictive value (NPV)
  - Incidence (acute HIV)

STATUS

- 78/200 enrolled
- 19 HIV positive

TransViiV

Inclusion criteria: 60 HIV-1 naive, ≥18 years old, self identified as TGW



Status:
In screening: 18
Enrolled and commenced on treatment: 10

Team

Transhotel
Consultorio inclusivo

Recursos

- ✓ Remuneracion del equipo
- ✓ Costo de atención
- ✓ Costo de los procedimientos
- ✓ Costo de Laboratorio
- ✓ Recolección, monitoreo y análisis de datos
- ✓ Personal de apoyo
- ✓ Viajes y congresos
- ✓ Publicaciones

INFRAESTRUCTURA

Espacio

pacientes

procedimientos

CLINICA

POEs

COMITÉ DE ETICA

REGULATORIO

AE/SAE

Confidencialidad

DATOS

CRF

Calidad

Data entry

Estadístico

LABORATORIO

Kits

Back ups

Alertas

FARMACIA

Control T

Stock

Trazabilidad

Beneficios de la IC

- ✓ Participantes (No siempre)
- ✓ Sitio: Ordena la información
- ✓ Provee recursos materiales y económicos

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Que es el IP?

El investigador Principal es *"El lider de un equipo, responsable de la conduccion de la investigacion y y de las acciones de cualquier miembro de su equipo, con arreglo a las Buenas Practicas Clinicas"*

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Los trece principios de las Buenas Prácticas Clínicas

1.- Principios **éticos**, según la Declaración de Helsinki
2.- Evaluacion cuidadosa de los posibles **riesgos** y **beneficios**
3.- Proteger los **derechos, la seguridad y el bienestar de los sujetos**
4**.– Información adecuada** para apoyar la propuesta de realizar el estudio clínico.
5**.- Bases científicas razonables**.
6.-Aprobacion previa por un **Comité de Ética** Independiente.
7.- C**uidado** médico de los sujetos de la investigación
8.- El participante debe tener **la educación, el entrenamiento y la experiencia** adecuados
9.- **Consentimiento informado**
10.- **Información** documentada y archivada
11.- Proteger la **confidencialidad** de los datos de los participantes.
12.- Los productos de investigación deben ser fabricados, administrados y almacenados de acuerdo con la **Buena Práctica de fabricación industrial** (*Good Manufacturing Practice* – GMP).
13.- Establecer sistemas de **procedimientos** que aseguren la calidad de todos los aspectos del estudio clínico. (Responsabilidad del patrocinador y del investigador)

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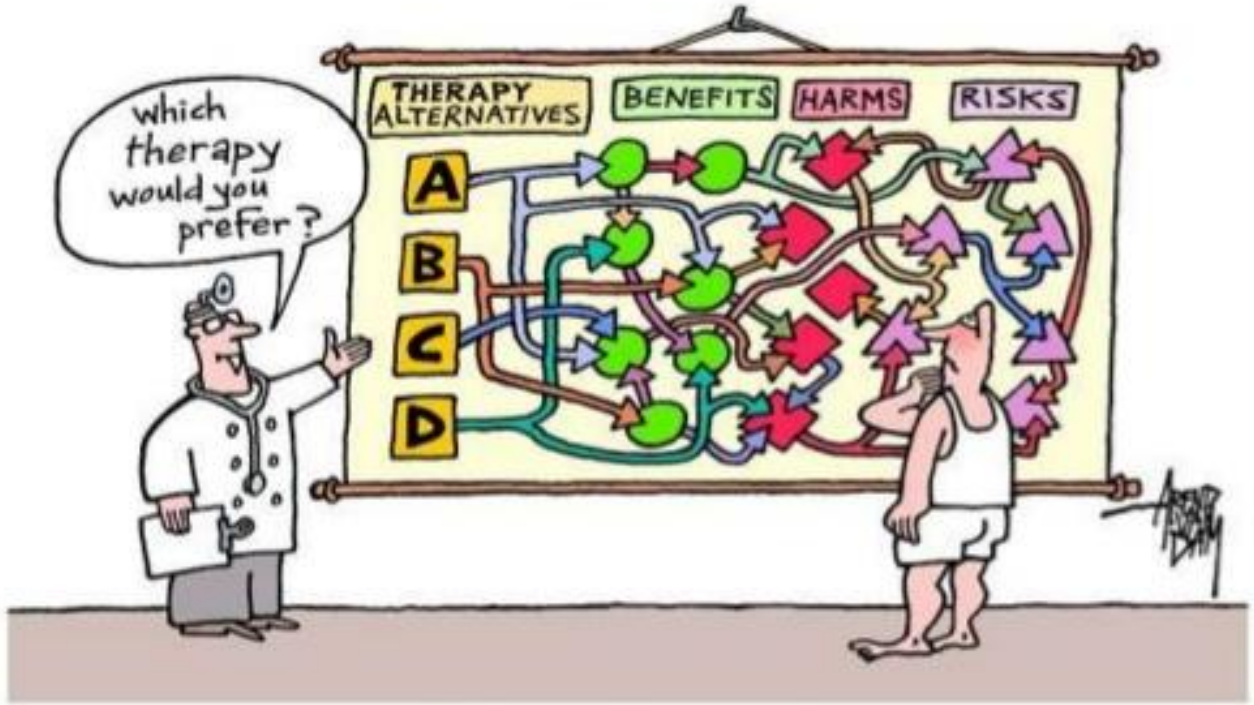
El investigador y el consentimiento informado

- El investigador o la persona designada debe:
  - Dar suficiente tiempo al sujeto para hacer una decisión, además de darle la oportunidad para hacer preguntas y finalmente decidir si participa o no en el estudio.

INFORMED CONSENT



informed consent

El investigador y el consentimiento informado

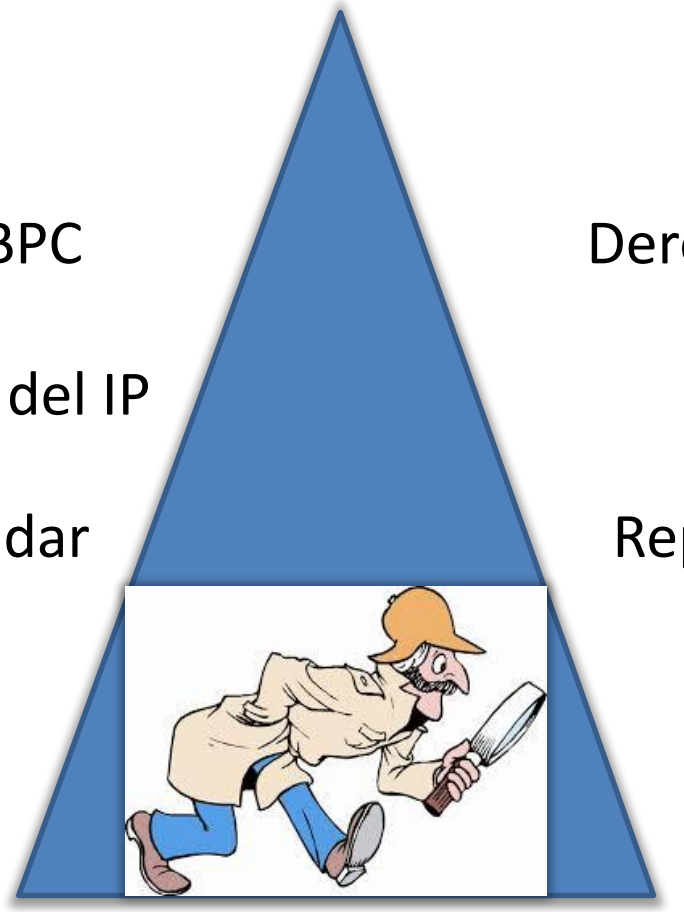
- El investigador o la persona designada debe:
  - Informar exhaustivamente al sujeto de todos los aspectos del ensayo clínico.
  - El lenguaje usado en el consentimiento informado
    - No debe ser técnico
    - Debe ser práctico
    - De fácil entendimiento para el sujeto y el testigo imparcial.

En síntesis, el IP debe garantizar….

Observación de las BPC

Responsabilidad final del IP

Procedimientos estándar



Derechos protegidos

Datos precisos

Reportes confiables

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Investigación en Fundación Huesped
(al 31/08/19)

- ✓ Estudios de la industria, cooperativos intercentros, redes internacionales e iniciativa del investigador (II).
- ✓ A la fecha: 187 estudios clínicos, 44 II
- ✓ Pacientes incluidos: 2806, randomizados: 1913
- Participación en redes de investigación del NIH: IMPAACT, HPTN, COPA, CCSANeT, AMC, U54, HVTN

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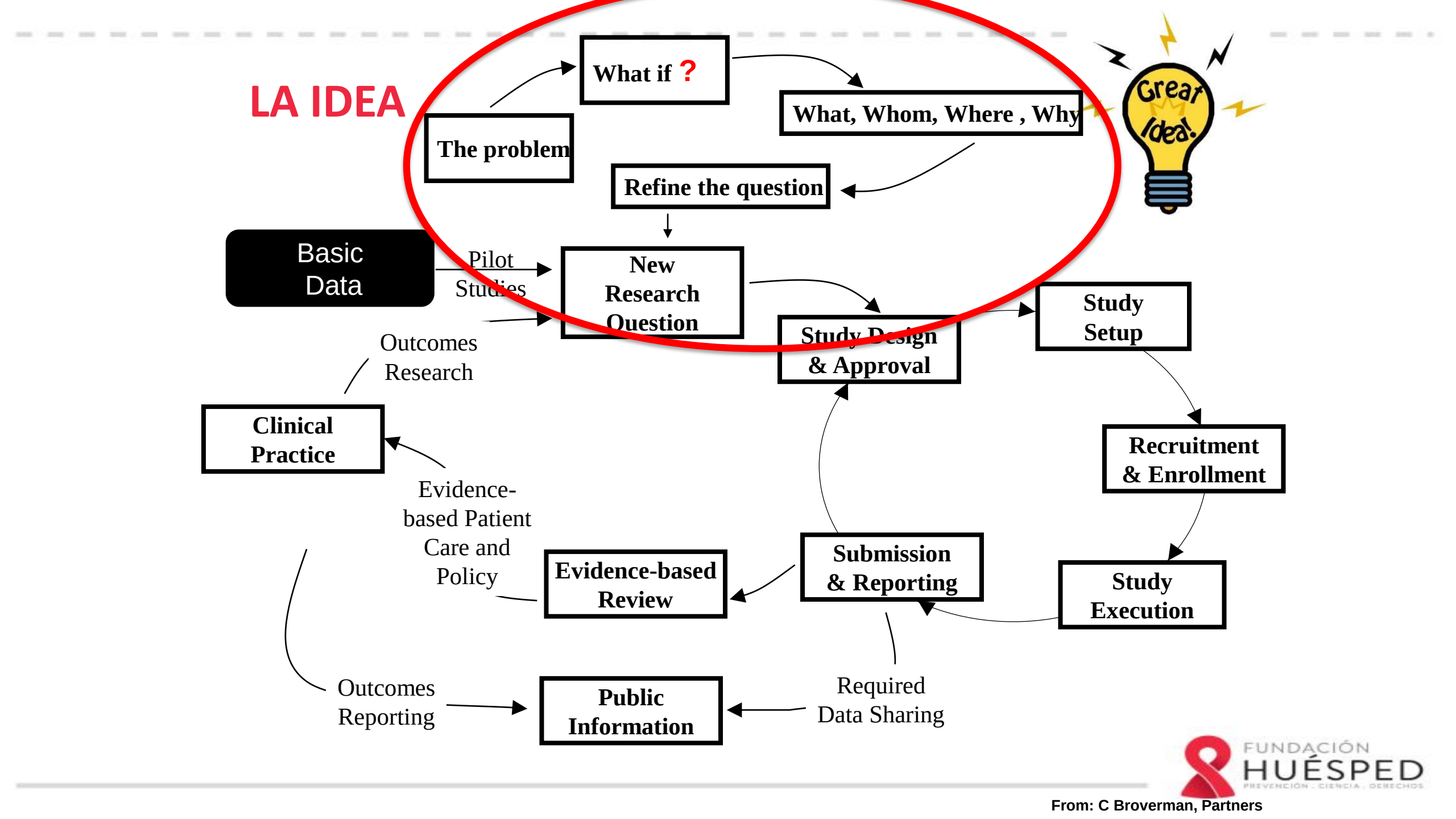
UEM-GARDEL

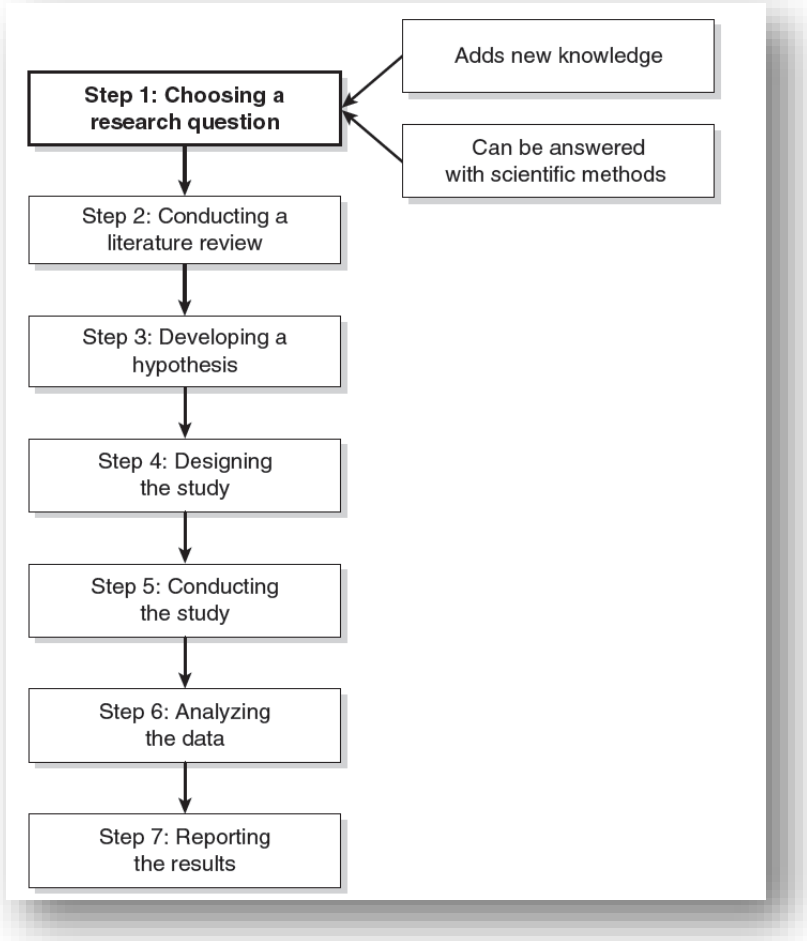
- Unidad de Estudios Multicéntricos GARDEL, donde se desarrollan y coordinan estudios clínicos a iniciativa del investigador.
- Creada para organizar y coordinar el estudio GARDEL
- Actualmente coordina estudios de iniciativa local (ANDES, TRANS-VIIV, PADDLE) y estudios internacionales (COPA 2, HPTN-083, HVTN, AMC, U-54)
- Ejerce el control de calidad y monitoreo internos

LA IDEA



From: C Broverman, Partners

La pregunta = La idea



La pregunta debe ser:

- Importante para ganar conocimiento
- Que se pueda responder con método cientifico
- No contestada antes

Factibilidad, innovación, novedad, etica, relevancia, pertinencia.

Dawn M. McBride - The Process of Research in Psychology, 2nd Edition © 2013 SAGE Publications, Inc.

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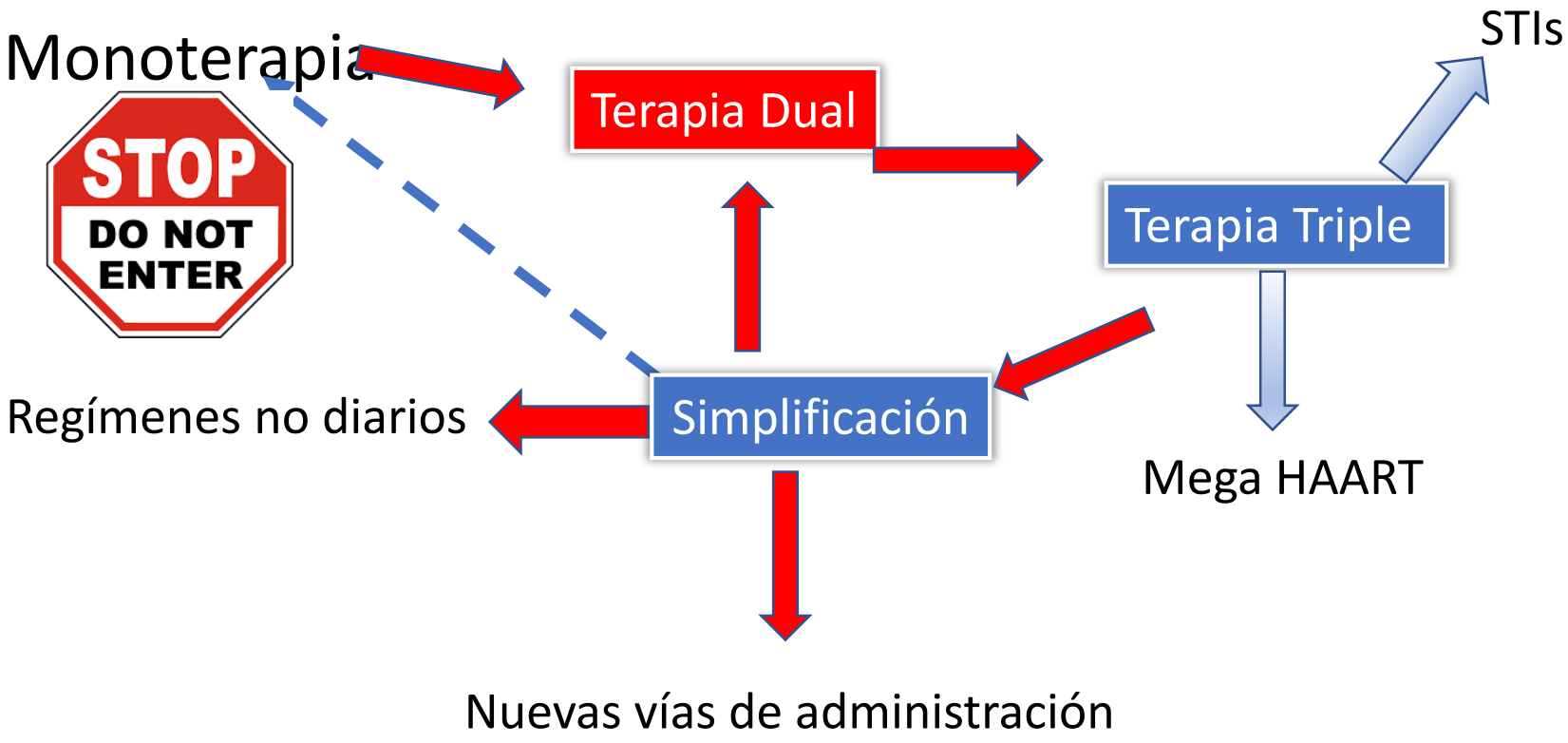
HAART: Es el numero de drogas o la eficacia y seguridad?

Estrategias de tratamiento: Un largo camino……



Por que reducir la carga de drogas?

- ✓ To reduce ARV exposure making treatment safer without sacrificing virologic control
- ✓ To reduce pill burden/improved patient adherence and quality of life
- ✓ To reduce drug-drug interactions
- ✓To reduce cost
- ✓Potential for longer-term success
  - ✓Downstream options with “spared” class in case of first-regimen failure

Reduccion de la carga de drogas:
Desventejas potenciales

- ✓ Reduced potency?
- ✓ Less forgivness for missing doses?
- ✓ Reduced penetration in sanctuaries?
- ✓ More frequent viral load monitoring?
- ✓ Less durability?
- ✓ Loss of TDF lipid-lowering effect
- ✓ Contraindicated in HBV coinfection (*3TC-based DT*)

Terapia dual: no siempre exitosa

- **LPV/r - EFV**
- **ATV/r - EFV**
- **LPV/r - NVP**

Good virological response, but increased rate of side effects

- **ATV 300 mg BID + RAL (SPARTAN)**
- **MVC QD + DRV/RTV (MODERN)**
- **DRV/r + RAL (ACTG 5262)**
- **DRV/r + RAL (NEAT 001)***
- **ATV/r + RAL (HARNESS – switch)**
- **MARAVIROC+ bPI (MARCH -Switch)**

*** Strata high pVL and/or low CD4**

Lamivudine

- Once daily NRTI
- Very well tolerated
  - Almost no side effects reported
- No drug-drug interactions
- Generic, low cost
- Low genetic barrier, selects M184V or I
- Residual antiviral activity even after selecting the mutation
- Enhances antiviral activity of TDF and ZDV

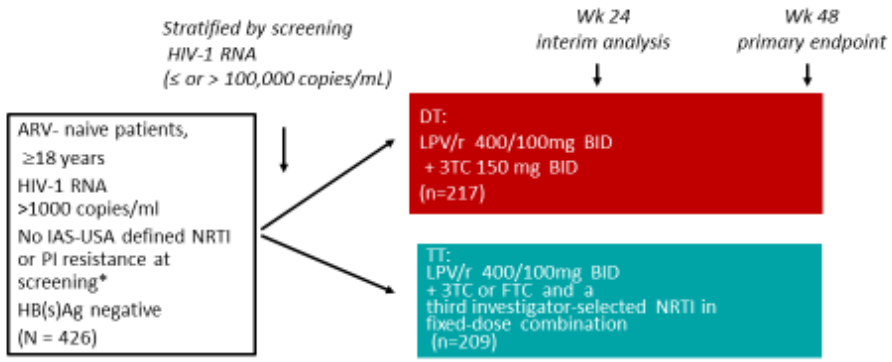
GARDEL

First full powered study to provide evidence of dual therapy compared to triple therapy among HIV naive individuals

IP/r + 3TC
GARDEL

Phase III, randomized, international , controlled, open-label study

- Study included adult patients from Argentina, Chile, Mexico, Peru, Spain, US.



*Defined as ≥ 1 major or ≥ 2 minor LPV/r mutations)
LPV major mutations include the following mutations: V32I; I47V/A; L76V; V82A/F/T/S

Cahn, Lancet Inf. Dis, 2014

Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents

Lopinavir/Ritonavir plus Lamivudine

In the GARDEL study, 426 ART-naive patients were randomized to receive twice-daily LPV/r plus either open-label 3TC (twice daily) or two NRTIs selected by the study investigators. At 48 weeks, a similar number of patients in each arm had HIV RNA <50 copies/mL, meeting the study's non-inferiority criteria. The LPV/r plus 3TC regimen was better tolerated than the LPV/r plus 2 NRTI regimen.[88]

An important limitation of the GARDEL study is the use of LPV/r, twice daily dosing, and relatively high pill burden (total of 6 tablets per day). LPV/r is not considered a Recommended or Alternative initial PI because of its unfavorable adverse event and pill burden characteristics as compared to pharmacokinetically enhanced ATV and DRV. Given the above limitations, the Panel recommends that LPV/r plus 3TC be considered for use only in patients who cannot take either TDF or ABC (**CI**).

In summary, the aggregate results from these two fully powered studies with NRTI-limiting regimens demonstrate that these initial strategies have significant deficiencies as compared to standard-of-care treatment approaches, in particular, disadvantages related to pill burden or dosing frequency. In addition, there are concerns about the virologic efficacy of DRV/r plus RAL in patients with high viral loads or low CD4 cell counts. The Panel only recommend LPV/r plus 3TC or DRV/r plus RAL for initial therapy when both TDF and ABC are contraindicated. Other less well-tested NRTI-limiting combinations are not recommended.

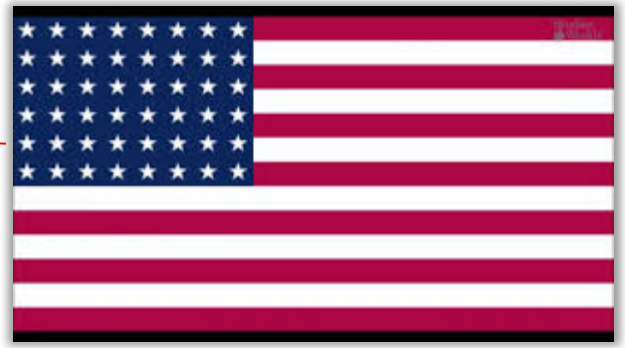
Documento de consenso de GeSIDA/Plan Nacional sobre el Sida respecto al tratamiento antirretroviral en adultos con infección por el virus de la inmunodeficiencia humana

(Actualización enero 2015)

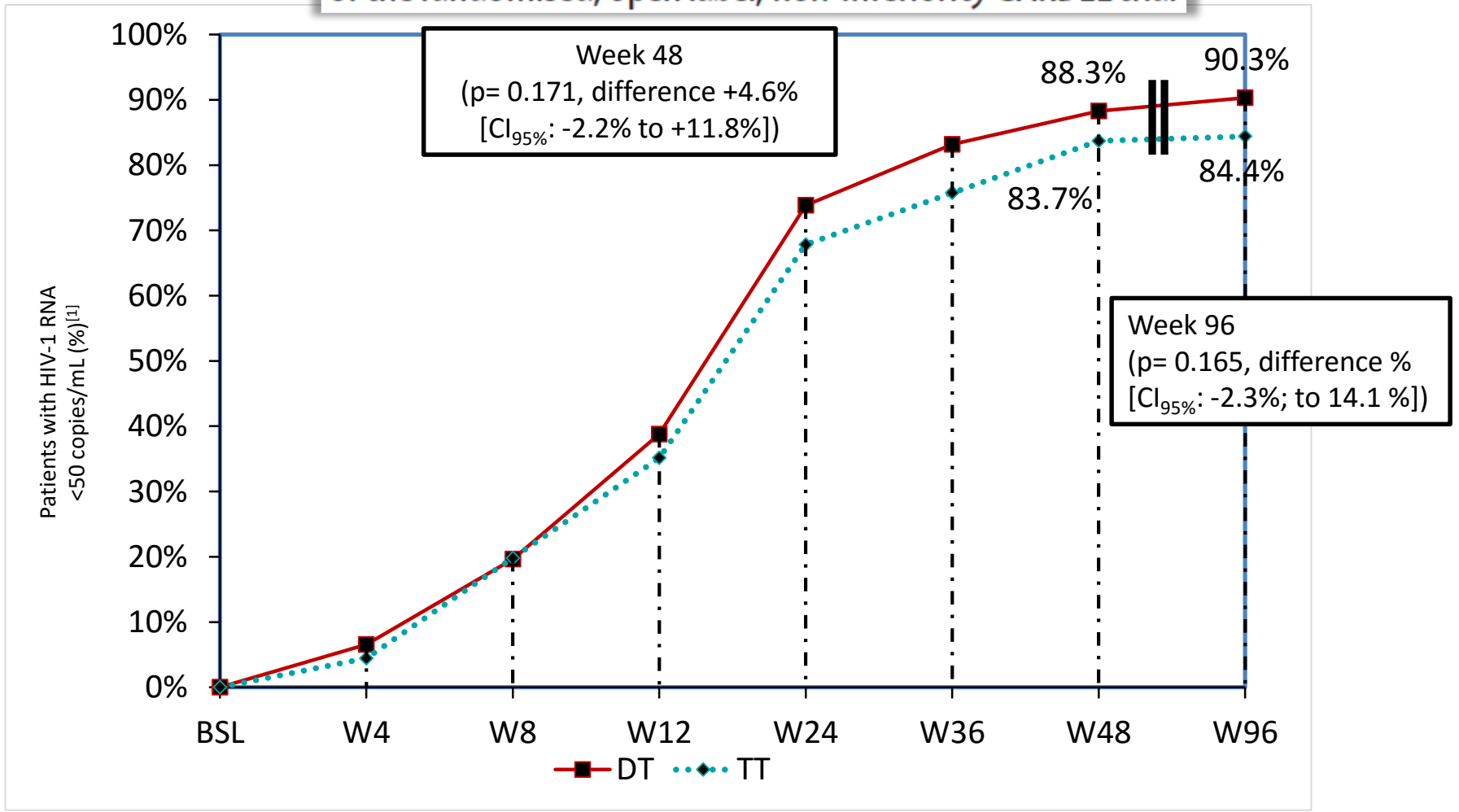
Recomendaciones

- Los regímenes basados en IP recomendados son DRV/r (o DRV/COBI) QD + TDF/FTC y ATV/r (o ATV/COBI) QD + TDF/FTC ***(A-I)***. La combinación de ATV/r (o ATV/COBI) + ABC/3TC también se recomienda, pero se debe evitar en pacientes con CVP superior a 100.000 co-pias/mL ***(A-I)***
- Otras pautas con IP incluyen LPV/r, BID o QD, + TDF/FTC o ABC/3TC ***(B-I)***. Es posible utilizar también la combinación DRV/r (o DRV/COBI) + ABC/3TC, aunque no ha sido formalmente investigada en ningún ensayo clínico ***(B-III)***
- ATV y DRV pueden ser potenciados indistintamente con 100 mg de RTV o 150 mg de COBI ***(B-II)***
- LPV/r + 3TC, LPV/r + RAL y DRV/r + RAL pueden ser una alternativa a la triple terapia con-vencional cuando no se pueda utilizar TDF ni ABC ***(B-I)***. Las pautas dobles sin ITIAN (DRV/r

GARDEL:
18 centros
535 pacientes



Dual therapy with lopinavir and ritonavir plus lamivudine versus triple therapy with lopinavir and ritonavir plus two nucleoside reverse transcriptase inhibitors in antiretroviral-therapy-naive adults with HIV-1 infection: 48 week results of the randomised, open label, non-inferiority GARDEL trial



Pedro Cahn, Jaime Andrade-Villanueva, José R Arribas, José M Gatell, Javier R Lama, Michael Norton, Patricia Patterson, Juan Sierra Madero, Omar Sued, Maria Inés Figueroa, Maria José Rolon, on behalf of the GARDEL Study Group*

Lancet Infect Dis 2014

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ESTUDIO ANDES
DRV/RTV/3TC COMBINADOS PARA EXPLORAR TOLERABILIDAD, EFICACIA Y SEGURIDAD

UEM GARDEL
UNIDAD DE ESTUDIOS MULTICÉNTRICOS

ANDES

A Phase 4, Randomized, Open Label, Study of a Ritonavir-Boosted Darunavir in Fixed Dose Combination (FD-DRV/r) plus Lamivudine Versus FD-DRV/r plus Lamivudine/Tenofovir in Naïve HIV-1 Infected Subjects

Pedro Cahn on behalf of the ANDES Study Group

ClinicalTrials.gov : # **NCT02770508**

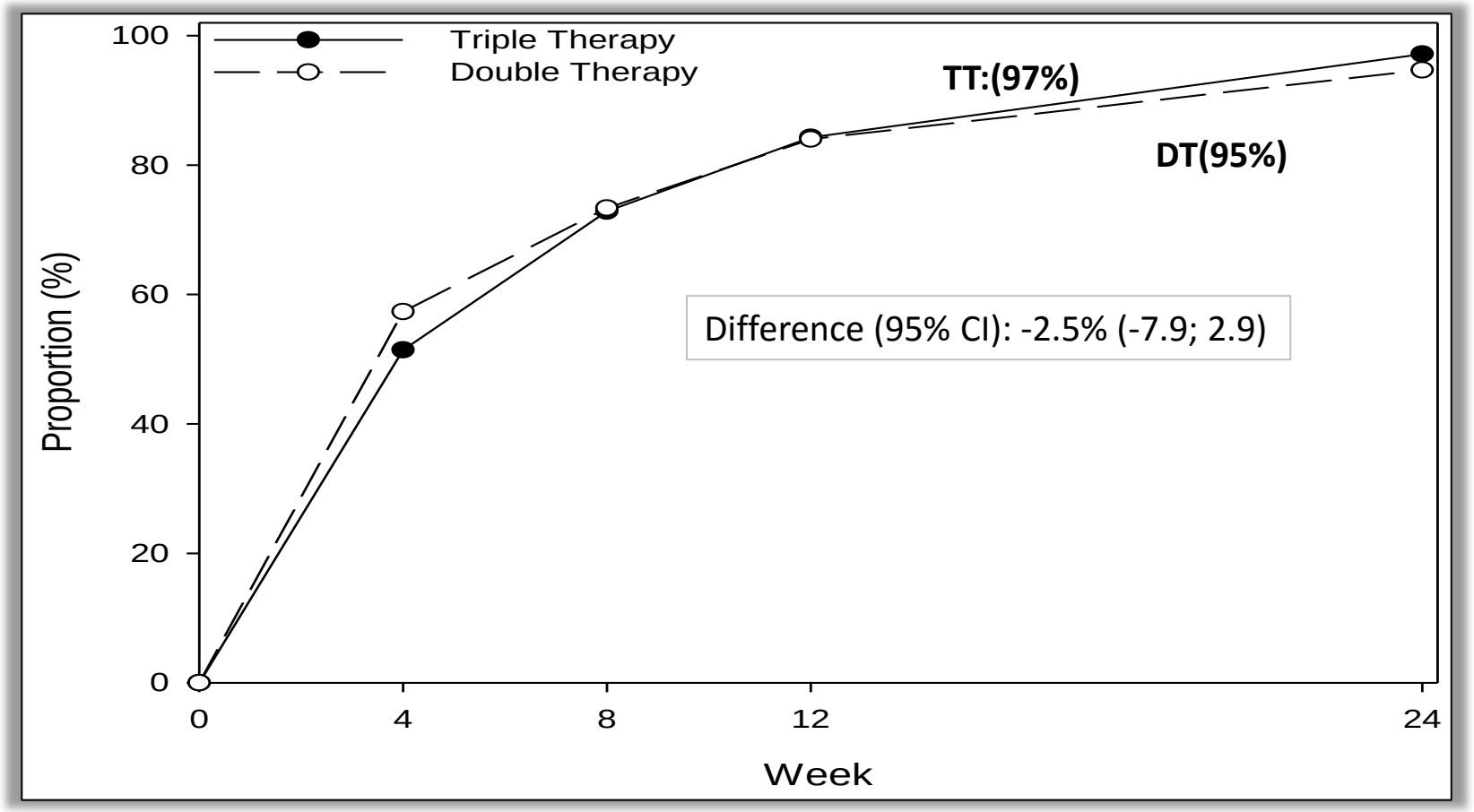
About this study

This is an investigator initiated study, designed, conducted and sponsored by Fundación Huésped.

Funding sources: Ministry of Science and Technology, Ministry of Health and Richmond laboratories, Buenos Aires, Argentina

ESTUDIO ANDES
DRV/RTV/STC COMBINADOS PARA EXPLORAR TOLERABILIDAD, EFICACIA Y SEGURIDAD

Viral load <400 copies/mL at week 24 ,ITT snapshot, (n=145)



Proportion of patients with plasma HIV-1 RNA less than 400 copies per mL

Mean CD4+ increases were similar in both arms
(DT=206 cells/mm3; TT=204 cells/mm3).

Estudio ANDES

FUNDACIÓN HUÉSPED
PREVENCIÓN-CIENCIA-DERECHOS

ID *489*

DRV/R FDC plus 3TC for HIV-1 treatment naive patients: Week 48 results of the ANDES study

Authors:, Maria I. Figueroa[1], Omar G. Sued[1], Ana M. Gun[1], Waldo H. Belloso[2], Diego M. Cecchini[3], Gustavo Lopardo[4], Daniel Pryluka[5], Maria J. Rolon[1], Valeria I. Fink[1], Santiago Perez Lloret[6], **Pedro Cahn[1]**
[1]Fundación Huésped, [2]Hospital Italiano, [3]Hospital Argerich,[4]Centro de Estudios Infectológicos,, [5]Consultorio Infectológico,, [6]University of Buenos Aires, all in Buenos Aires, Argentina

- **Background**: Dual therapy has been explored in different studies. A generic fixed dose combination (FDC) of DRV800/ritonavir100 mg is available in Argentina. We designed a study to compare efficacy and safety of this FDC plus 3TC to standard-of care HAART based on the same drugs plus tenofovir. ClinicalTrials.gov Identifier: NCT02770508
- **Methods**:ANDES is a randomized, open-label, phase IV study, designed to compare dual therapy (DT) with DRV/RTV (800/100 mg) FDC, plus 3TC (300 mg), to triple therapy (TT) with DRV/RTV (800/100 mg) plus 3TC/TDF (300/300mg),FDC in treatment-naïve HIV-1 infected patients. Primary endpoint: proportion of patients with viral load (pVL) <50 copies/mL at week 48 (FDA snapshot -ITTe analysis) Preplanned week 24 analysis was presented at IAS 2017.Week 48 results are reported here.
- **Results**: Out of 182 patients screened, 145 were randomized to receive: DT (n75) or TT (n70). At baseline 92% were on CDC stage A: 24% had pVL> 100,000 copies/mL(table 1). At week 48, 93 % of patients on DT and 94% on TT achieved pVL <50 copies/mL, difference (95% CI): -1.0% (-7.5; 5.6%). 92% of patients with baseline pVL>100,000 copies/mL showed 92% response in TT arm and 91% in DT. (figure 1 and table 2) One patient presented virological failure at W48 (TT arm).Per-protocol analysis: 99% were responders in TT arm and 100% in DT arm. Median CD4+ change between BSL and week 48 was similar in both arms (TT: 200 cells/mm3; DT:246 cells/mm3; (p:0.20)(figure 2) Thirty six grade 2-4; possible/probable related adverse events (AEs)were reported among 28 patients(TT:17;DT:11), the most frequent AEs were gastrointestinal (TT: 14%; DT: 7%; p:0.17) and rash (TT:7%; DT: 8%;p:0.95). Laboratory abnormalities were similar in both arms except regarding total cholesterol (change from BSL to W48: TT: 4%; DT: 19%; p: 0.01).LDL-cholesterol and triglycerides showed a non-significant trend in favor of TT(TT: 6%/DT 14% and TT: 14%/DT: 25% respectively. AEs leading to discontinuation were rare and similar between arms. No treatment-related SAEs or deaths were reported
- **Conclusion**: A generic FDC of DRV/RTV plus 3TC showed non-inferiority to a standard of care triple drug regimen with ritonavir-bosted Darunavir in FDC plus TDF/3TC at 48 weeks.This study adds further evidence about the efficacy of drug-sparing regimens in treatment-naïve patients

Table 1. Demographics at screening

	Global (n=145)	Triple therapy (n=70)	Double therapy (n=75)
Age	33.1±9.9	32.5±8.4	33.7±11.1
	30 (25.5–39.5)	30 (26–38)	30 (24–42)
Males	131 (91%)	61 (88%)	70 (94%)
Hispanic/Latino	102 (71%)	49 (71%)	53 (71%)
MSM/Bisexual	101 (70%)	48 (71%)	53 (76%)
CDC Stage B	11 (8%)	5 (7%)	6 (8%)
Viral Load (log)	4.5 (4.0–5.0)	4.5 (3.9–5.0)	4.6 (4.1–5.1)
CD4 count	383 (286–562)	366.5 (275–564)	419 (290–564)
CD4 %	19 (14–25)	19 (14–25)	19 (14–25)
VL >100000 c/mL (Baseline)	35 (24%)	15 (22%)	20 (27%)

* All patients were on CDC stage A or B

Figure 1. Proportion of patients with plasma HIV-1 RNA less than 50 copies/mL

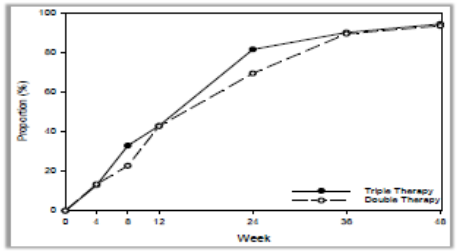


Figure 2 :CD4 count increase (means ± standard error of the mean)

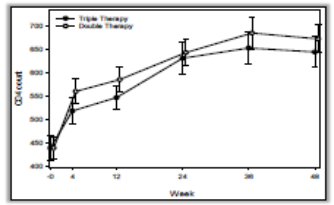


Table 2. Efficacy analysis

	Global	Triple therapy	Double therapy	Difference (95% CI)
Primary outcome: VL<50 c/mL at week 48				
ITT snapshot, (n=145)	136 (94%)	66 (94%)	70 (93%)	-1.0% (-7.5 ; 5.6%)
ITT snapshot, baseline VL > 100.000 c/ml (n=35)	32 (91%)	12 (92%)	20 (91%)	-1.4% (-17.2 ; 14.4%)
Observed (n=140)	136 (99%)	66 (99%)	70 (100%)	1.5% (-0.9% ; 3.9%)

Correspondence:pcahn@huesped.org.ar

ESTUDIO ANDES

Figueroa, CROI 2018

Financiacion conjunta: MinSAL, MINCyT, Lab Richmond

Cahn P et al. *Journal of the International AIDS Society* 2017, **20**:21678
http://www.jiasociety.org/index.php/jias/article/view/21678 | https://doi.org/10.7448/IAS.20.1.21678

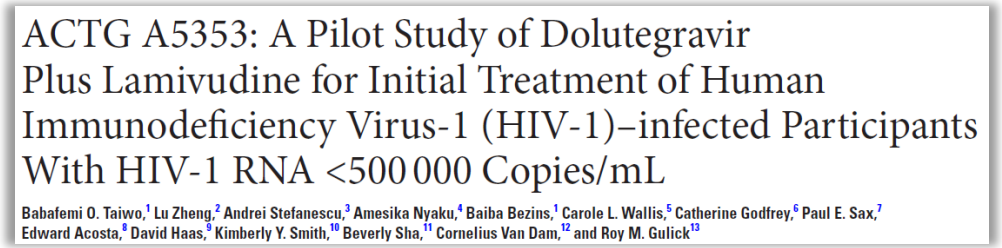
JIAS Journal of the International AIDS Society

Research article

Dolutegravir–lamivudine as initial therapy in HIV-1 infected, ARV-naive patients, 48-week results of the PADDLE (Pilot Antiretroviral Design with Dolutegravir LamivudinE) study

Pedro Cahn[§1], María José Rolón[1], María Inés Figueroa[1], Ana Gun[2], Patricia Patterson[1] and Omar Sued[1]

[§]Corresponding author: Pedro Cahn, Fundación Huésped, Buenos Aires C1202ABB Argentina. (pedro.cahn@huesped.org.ar)



ACTG A5353: A Pilot Study of Dolutegravir Plus Lamivudine for Initial Treatment of Human Immunodeficiency Virus-1 (HIV-1)–infected Participants With HIV-1 RNA <500 000 Copies/mL

Babafemi O. Taiwo,[1] Lu Zheng,[2] Andrei Stefanescu,[3] Amesika Nyaku,[4] Baiba Bezins,[1] Carole L. Wallis,[5] Catherine Godfrey,[6] Paul E. Sax,[7] Edward Acosta,[8] David Haas,[9] Kimberly Y. Smith,[10] Beverly Sha,[11] Cornelius Van Dam,[12] and Roy M. Gulick[13]

#W96	SCR	BSL	DAY 4	DAY 7	W.2	W.3	W.4	W.6	W.8	W.12	W.24	W.36	W.48	W 96
1	5.584	10.909	383	101	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50
2	8.887	10.233	318	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50
3	67.335	151.569	1.565	1.178	97	53	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50
4	99.291	148.370	3.303	432	178	55	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50
5	34.362	20.544	1.292	570	107	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50
6	16.024	14.499	1.634	162	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50
7	37.604	18.597	819	61	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50
8	25.071	24.368	1.377	Not done	105	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50
9	14.707	10.832	516	202	< 50	< 50	< 50	< 50	< 50	< 50	< 50	SAE		
10	10.679	7.978	318	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50	<50
11	50.089	273.676	68.129	3.880	784	290	288	147	< 50	< 50	< 50	< 50	< 50	70/<50 *
12	13.508	64.103	3.296	135	351	84	67	< 50	< 50	< 50	< 50	< 50	< 50	< 50
13	28.093	33.829	26.343	539	61	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50
14	15.348	15.151	791	198	< 50	61	64	< 50	< 50	< 50	< 50	< 50	< 50	< 50
15	23.185	23.500	4.217	192	< 50	< 50	< 50	Not done	< 50	< 50	< 50	< 50	< 50	< 50
16	11.377	3.910	97	143	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50
17	39.100	25.828	1.970	460	52	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50
18	60.771	73.069	2.174	692	156	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50
19	82.803	106.320	2.902	897	168	76	< 50	< 50	< 50	< 50	< 50	PDVF		
20	5.190	7.368	147	56	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50	<50

ITT-e: 90% < 50 copies/mL at W 48 & 96
Observed data: 95% <50 copies/mL
n=1 with PDVF; No mutations detected

Cahn: JIAS 2017

Virologic Outcome at Wk 24, n (%) [Primary endpoint]	Baseline HIV-1 RNA, copies/mL		Total (N = 120)
	> 100,000 (n = 37)	≤ 100,000 (n = 83)	
Success (pVL<50 copies/mL)	33 (89)	75 (90)	108 (90)
Nonsuccess	3 (8)	2 (2)	5 (4)
No data	1 (3)	6 (7)	7 (6)

n = 3 with PDVF; n = 1 with emergent M184V and R263RK

ITT-e: 90% < 50 copies/mL at W 24

Taiwo: CID 2018,

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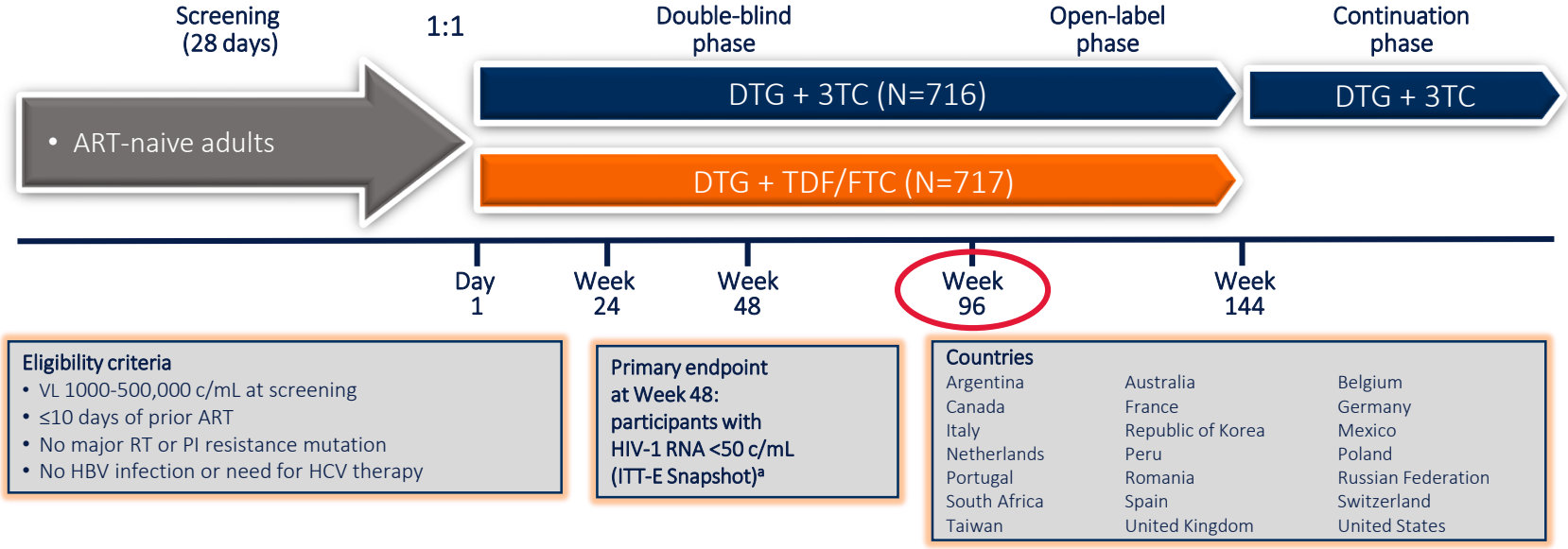
GEMINI-1 AND GEMINI-2 PHASE III STUDY DESIGN

Identically designed, randomized, double-blind, parallel-group, multicenter, non-inferiority studies

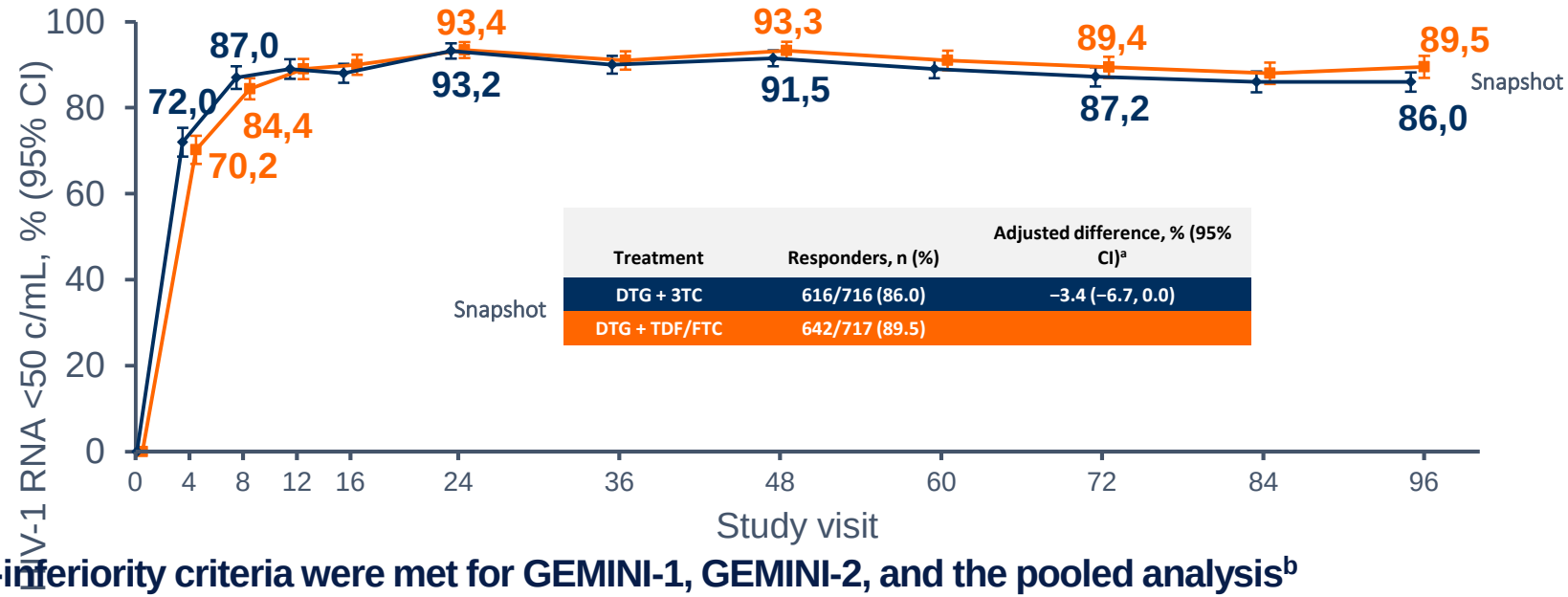


Baseline stratification factors: plasma HIV-1 RNA (≤100,000 vs >100,000 c/mL) and CD4+ cell count (≤200 vs >200 cells/mm^3).

[a]–10% non-inferiority margin for individual studies.

Cahn et al. IAS 2019; Mexico City, Mexico. Slides WEAB0404LB.

DTG + 3TC IS NON-INFERIOR TO DTG + TDF/FTC IN SNAPSHOT HIV-1 RNA <50 C/ML AT WEEK 96



	Treatment	Responders, n (%)	Adjusted difference, % (95% CI)[a]
Snapshot	DTG + 3TC	616/716 (86.0)	−3.4 (−6.7, 0.0)
	DTG + TDF/FTC	642/717 (89.5)	

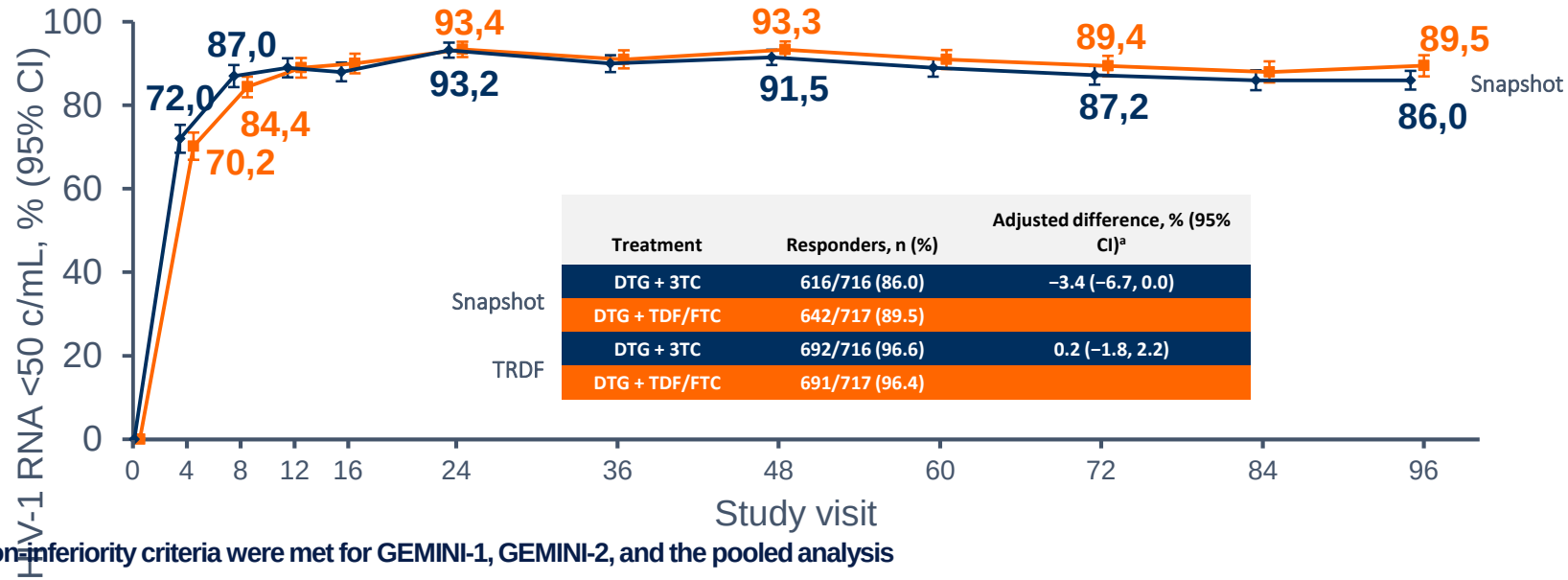
Non-inferiority criteria were met for GEMINI-1, GEMINI-2, and the pooled analysis[b]

[a]Based on Cochran-Mantel-Haenszel stratified analysis adjusting for the following baseline stratification factors: plasma HIV-1 RNA (≤100,000 vs >100,000 c/mL), CD4+ cell count (≤200 vs >200 cells/mm^3), and study (GEMINI-1 vs GEMINI-2). The upper limit of the 95% CI for the pooled analysis was 0.0007%.

[b]In GEMINI-1, HIV-1 RNA <50 c/mL (95% CI) was achieved in 300/356 participants (84.3% [80.5-88.1]) in the DTG + 3TC group and 320/358 (89.4% [86.2-92.6]) in the DTG + TDF/FTC group (adjusted treatment difference [95% CI], −4.9% [−9.8, 0.03]). In GEMINI-2, the corresponding values were 316/360 (87.8% [84.4-91.2]) and 322/359 (89.7% [86.5-92.8]), respectively (adjusted treatment difference [95% CI], −1.8% [−6.4, 2.7]).

Cahn et al. IAS 2019; Mexico City, Mexico. Slides WEAB0404LB.

DTG + 3TC IS NON-INFERIOR TO DTG + TDF/FTC IN SNAPSHOT HIV-1 RNA <50 C/ML AT WEEK 96



	Treatment	Responders, n (%)	Adjusted difference, % (95% CI)[a]
Snapshot	DTG + 3TC	616/716 (86.0)	−3.4 (−6.7, 0.0)
	DTG + TDF/FTC	642/717 (89.5)	
TRDF	DTG + 3TC	692/716 (96.6)	0.2 (−1.8, 2.2)
	DTG + TDF/FTC	691/717 (96.4)	

- **Non-inferiority criteria were met for GEMINI-1, GEMINI-2, and the pooled analysis**
- **Treatment related discontinuation = failure (TRDF) population accounts for confirmed virologic withdrawal, withdrawal due to lack of efficacy, withdrawal due to treatment-related AE, and participants who met protocol-defined stopping criteria**

[a]Based on Cochran-Mantel-Haenszel stratified analysis adjusting for the following baseline stratification factors: plasma HIV-1 RNA (≤100,000 vs >100,000 c/mL), CD4+ cell count (≤200 vs >200 cells/mm^3), and study (GEMINI-1 vs GEMINI-2). The upper limit of the 95% CI for the pooled analysis was 0.0007%. TRDF (unadjusted difference) was a pre-planned analysis at Week 96.

[b]In GEMINI-1, HIV-1 RNA <50 c/mL (95% CI) was achieved in 300/356 participants (84.3% [80.5-88.1]) in the DTG + 3TC group and 320/358 (89.4% [86.2-92.6]) in the DTG + TDF/FTC group (adjusted treatment difference [95% CI], −4.9% [−9.8, 0.03]). In GEMINI-2, the corresponding values were 316/360 (87.8% [84.4-91.2]) and 322/359 (89.7% [86.5-92.8]), respectively (adjusted treatment difference [95% CI], −1.8% [−6.4, 2.7]).

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CONCLUSIONS

Durability

- DTG + 3TC maintained non-inferior efficacy over 96 weeks vs DTG + TDF/FTC in ART-naive adults

Barrier to Resistance

- Low rates of confirmed virologic withdrawal through Week 96, and no resistance development in either arm

Safety

- Overall safety and tolerability were comparable between groups
- Lower risk of drug-related AEs with DTG + 3TC
- Change in renal and bone biomarkers significantly favors DTG + 3TC
- Improvements in TC:HDL ratio in both arms

These results confirm DTG + 3TC is a compelling treatment option for PLWH

April 2019

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Conclusiones

- La IC aporta al progreso de la medicina
- Equipo, normas, recursos
- Acceso a población blanco
- Estricto respeto de las BPC
- Generar ideas y preguntas propias
- Trabajar metódicamente
- Admitir el posible fallo
- No bajar los brazos!
- Reclamar apoyo publico y privado para financiar la investigación!

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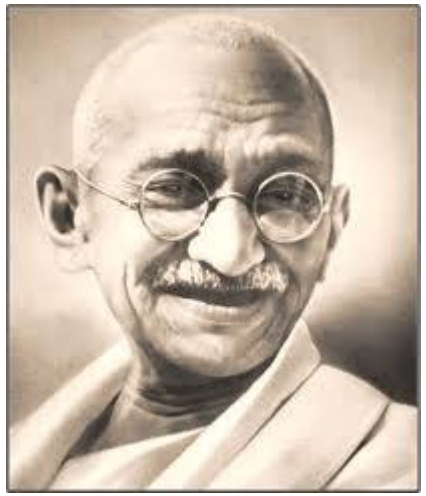
Que esperamos los investigadores de la sociedad?

Presupuesto apropiado!



"La India es un pais demasiado pobre para darse el lujo de no invertir en investigacion"

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GRACIAS POR LA ATENCION!

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