Partner Study

Investigator meeting EACS Belgrade
Thursday 13 October 2011
16.00-17.00 ~ Hyatt Regency

Welcome
Jens Lundgren

Agenda

1. Welcome
2. Enrollment status in PARTNER
3. New recruitment material
4. Presentation of the Community Lead initiative
5. Presentation of content of EACS poster
6. General discussion, experience at sites

Executive Committee

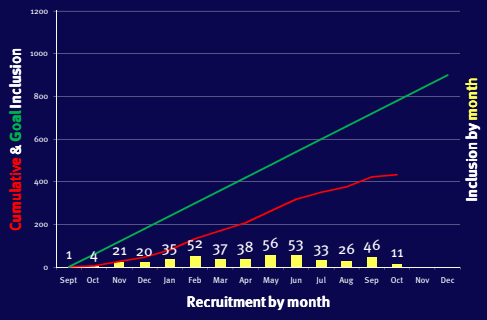
- Andrew Phillips, University College London (UCL)
- Jens Lundgren, University of Copenhagen and Rigshospitalet, Copenhagen, Denmark
- Alison Rodger, UCL
- Simon Collins, HIV i-Base, London
- Pietro Vernazza, Switzerland
- Vicente Estrada, Spain
- Jan Van Lunzen, Germany
- Tina Bruun, Copenhagen HIV Programme (CHIP)

National Coordinators

Amin Rieger,	Austria
Nathan Clumeck,	Belgium
Lars Mathiesen,	Denmark
Matti Ristola,	Finland
Christian Pradier,	France
Jan Van Lunzen,	Germany
Gráinne Courtney,	Ireland
Antonella d'Arminio Monforte,	Italy
Francisco Antunes,	Portugal
Vincente Estrada,	Spain
Katarina Westling,	Sweden
Pietro Vernazza,	Switzerland
JM Prins,	The Netherlands
Alison Rodger,	UK

Enrollment update,
Michelle Ellefson

Study update

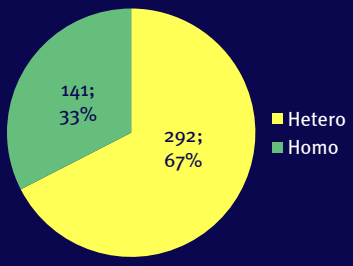


Study update

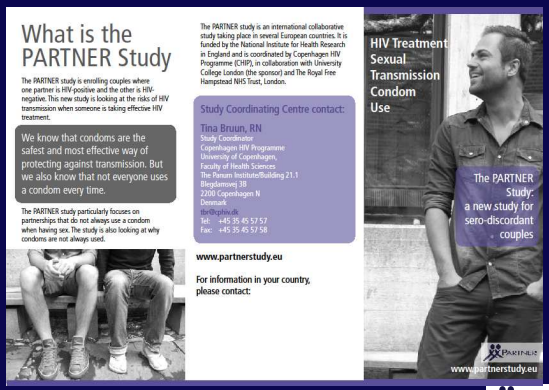
Country	Number of sites	Number open	Estimated	Enrolled	Percent of estimated goal
AT	4	3	60	19	31,7
BE	2	1	60	6	10,0
CH	5	5	125	64	51,2
DE	8	8	157	47	29,9
DK	4	4	67	29	43,3
ES	12	12	660	112	17,0
FI	1	1	20	8	40,0
FR	4	4	130	19	14,6
GB	19	17	500	77	15,4
IL	1	1	20	6	30,0
IT	3	3	95	9	9,5
NL	1	1	25	9	36,0
PT	1	0	20	0	0,0
SE	2	2	50	28	56,0
Total	67	62	1989	433	21,8

Study update

Proportion enrolled (433 pairs)



New Recruitment Material
Tina Bruun



Community Leads
Tina Bruun

Community Lead for the Partner study

- Italy: Giulio Maria Corbelli
- Spain: Michael Meulbroek
- Finland: Kimmo Karsikas
- Switzerland: David Haerry
- Portugal: Wim Vandevelde
- UK: Simon Collins
- Austria: Frank Michael Amort
-
- France:
- Belgium:
- Denmark:
- Germany:
- The Netherlands:
- Ireland:
- Sweden:

Tasks

- Informing community stake holders
- Provide information to gay/HIV media
- Provide the information on internet
- Arrange ways to distribute flyers, posters, ,,,
- Other activities to make the study known

Community Lead in Switzerland
David Haerry

EACS poster
Transmission Rates of HIV on Antiretroviral Therapy (ART): Unanswered Questions
Jens Lundgren

Background

- We know however that condom use is also highly effective at preventing HIV transmission, with reduction of transmission through the use of condoms alone in the region of 85% (95% CI: 60% - 96%)
- A key factor therefore to understand the effectiveness, (and hence cost-effectiveness) of an ART for prevention strategy is what is the absolute risk of HIV transmission through condom-less sex when the HIV-positive partner is on ART with a suppressed VL

Cohen et al NEJM 2011. 365(6):493-505.
Weller S et al. Cochrane Database Syst Rev. 2002;(1):CD003255.
Hughes J et al and the Partners in Prevention Study. CROI 2011, Paper # 135

Methods

We reviewed studies that reported risk of HIV transmission through condom-less sex when the HIV-positive partner is on ART with a suppressed VL

Results

- The HPTN 052 trial reported 1 linked transmission with suppressed VL (although even this may have been at higher VL) in 1585 couple-years in the early ART arm (0.1 per 100PY [0.0, 0.4])
- Similar findings have been reported in observational studies - 2009 meta-analysis reporting 0 transmissions in 291 couple-years on ART (from 2 studies) with VL<400 and a reduction in heterosexual transmission with ART of 92% from 5.64 to 0.46 per 100PY.
- Similarly the Partners in Prevention Study reported 1 transmission in 273 couple-years on ART (0.37 per 100PY [95% CI: 0.09, 2.004]) and the Rakai study reported 0 transmissions in 53.6PY (0 per 100PY [95%CI: 0, 5.98])

Cohen et al NEJM 2011. 365(6):493-505. AIDS. 2009. 17;23(11):1397-404. Donnell et al. Lancet 2010;375(9731):2092-8, Reynolds et al . AIDS. 2011.25(4):473-7, Mello et al. Sex Trans Dis. 2008. 35(11):912-5. Castilla et al J Acquir Immune Def Syndr. 2005. 40(1):96-101

Results - cont

- However it remains unclear what the risk of transmission is on ART when condoms are not used
- In studies to date most PY were without reported condom-less sex, so the low transmission risk is partly due to consistent condom use

Results - HIV transmission in serodiscordant coupes on ART and PY of follow up of condom less sex - cont

- Accounting for proportions having condom-less sex (around 4%, 75%, 7% and 46%) only approximately 329 couple-years of condom-less sex with VL suppression have been observed over all studies combined.
- Even with no transmissions (the two observed may not have been with VL suppression), this gives an upper 95% confidence for transmission of 1.1/100 couple-years.
- At least (if no transmissions) another 500 couple-years are needed to establish that the rate is below 0.5/100 couple-years.

Question is how low a risk of HIV transmission is considered an acceptable risk.

- Attia et al report the upper limit CI was equivalent to one new infection per 79 years of follow up (or one per 7900 sex acts if the yearly average is 100 contacts).
- Swiss Statement quoted risks of lower than 100,000 acts of sexual intercourse when the index on ART with undetectable VL and no STI.
- It is likely that an acceptable risk will be one that is at least twice that of an individual's life span i.e. 1 transmission per 200 years.
- If the true transmission rate is < 1 per 1000 person years, then 2000 PY with viral load < 50 will give upper 95% CI to be < 0.0044 (i.e. 1 per 227 person years of unprotected sex).

Conclusion

We know that transmission risk is reduced in people on ART with plasma viral load < 50 c/mL but it is critical to estimate how low this risk is.

Therefore further information in several areas is needed:

- More extensive study is required of sero-different couples having condom-less vaginal sex with suppressed VL on ART in order to more precisely estimate the risk of HIV transmission using ART alone
- There remains no data for anal sex in serodifferent MSM (and hetero) couples, which are likely to be different to vaginal sex, and ongoing studies that include MSM are critical.

Discussion: Site experiences

Site experiences

Dr. Gilles Wandeler Bern
Dr. Marcel Stoeckle - Basel

A new PARTNER Introduction presentation

Partner Study

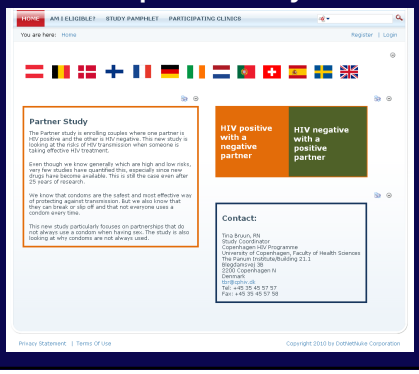
Partners of people on ART: a New Evaluation of the Risks (PARTNER study)

Includes slides for:

Introducing the study to potential participants

PARTNER: Website for study participants

www.partnerstudy.eu



Background

- People on ART with low viral load have markedly reduced infectiousness through sexual intercourse although the full extent of this is uncertain
- Increased interest in ART for prevention strategy following the results of the HPTN 052 RCT - 96% reduction in transmission
- We know however that condom use is also highly effective at preventing HIV transmission, with reduction of transmission through the use of condoms alone in the region of 85% (95% CI: 60% - 96%)
- A key factor therefore to understand the effectiveness, (and hence cost-effectiveness) of an ART for prevention strategy is what is the absolute risk of HIV transmission through condom-less sex when the HIV-positive partner is on ART with a suppressed VL

Cohen et al NEJM 2011. 365(6):493-505.
Weller S et al. Cochrane Database Syst Rev. 2002;(1):CD003255.
Hughes J et al and the Partners in Prevention Study. CROI 2011, Paper # 135

Conclusion

- We know that transmission risk is reduced in people on ART with plasma viral load < 50 c/mL but it is critical to estimate how low this risk is – in both heterosexual and MSM couples - if we are to understand the potential for widespread ART to reduce HIV incidence. T
- Therefore further information in several areas is needed.
  - More extensive study is required of sero-different couples having condom-less vaginal sex with suppressed VL on ART in order to more precisely estimate the risk of HIV transmission using ART alone
  - There remains no data for anal sex in serodifferent MSM couples, which are likely to be different to vaginal sex, and ongoing studies that include MSM are critical.

Results - HIV transmission in serodiscordant coupes on ART and PY of follow up of condom less sex

Author, Journal, Year	Type of study	Setting	VL lower limit of detection	PY follow up index case on HAART	Transmissions on ART	Estimated HIV transmission per 100PY (95% CI)	Proportion couples having condom-less sex	PY follow up index case on ART and having condom-less sex
Cohen [1] NEJM, 2011	Randomised controlled trial	Heterosexual couples, 13 sites in 9 countries	<400 copies/ml	1585.0	1	0.1 (0.0, 0.4)	4%	63.4
Attia, [4], AIDS, 2009	systematic review and meta-analysis	2 cohort studies included of sero-discordant heterosexual couples on ART with VL<400 [5,6]	<400 copies/ml	291.0	0	0 (0, 1.27)	75%	218.25
Donnell [7], Lancet, 2010	Observational cohort	Heterosexual couples, 14 sites in 7 African countries	240 copies per mL	273 .0	1 genetically linked HIV-1 transmission	0 37 (0 09, 2 04)	7%	19.1
Reynolds [8], AIDS.2011	Observational cohort	Heterosexual couples, Rakai study, Uganda	<400 copies/ml	68 .6	0	0 (0, 5 08)	46%	28.9