

# **HIV genotyping: yes or no?**

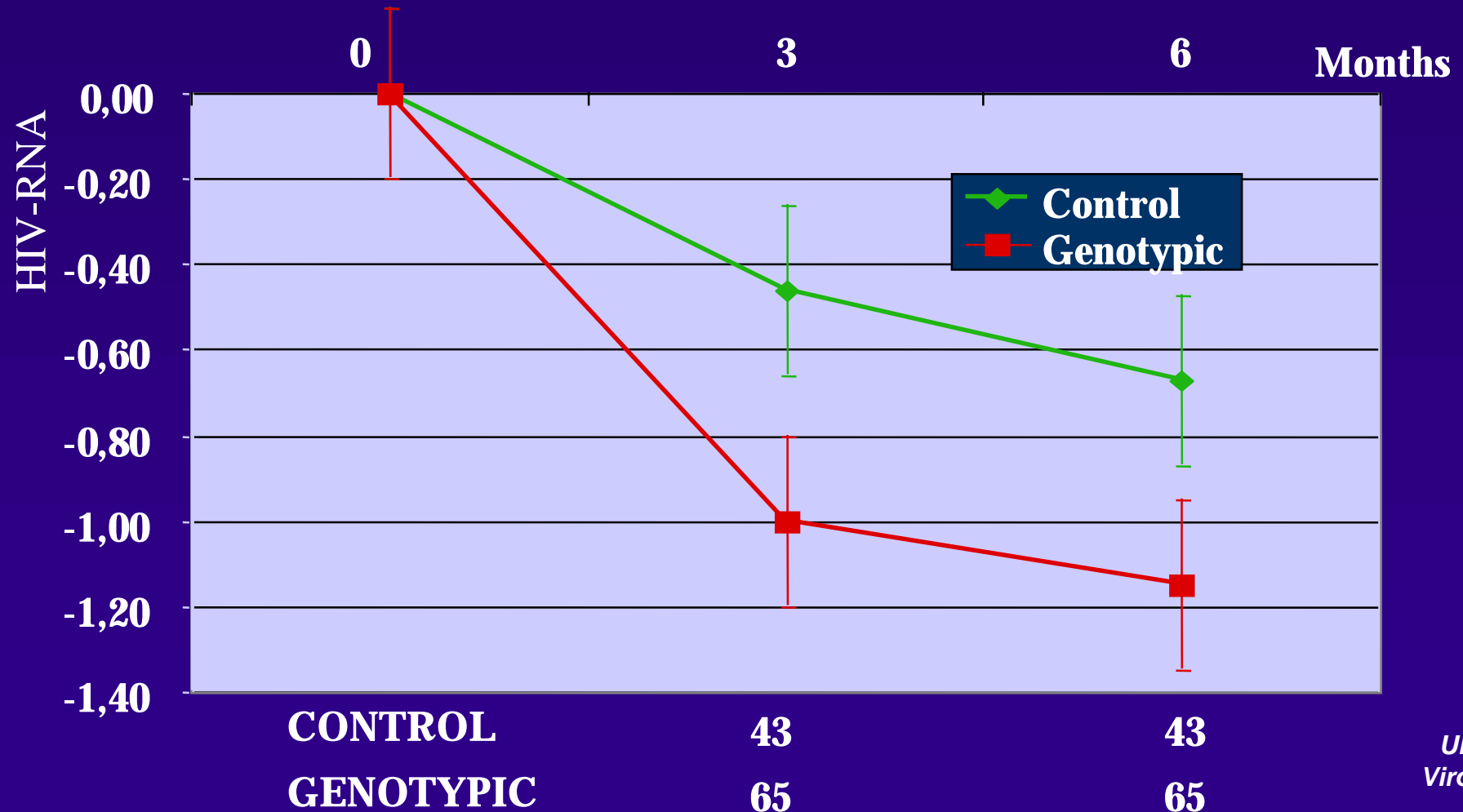
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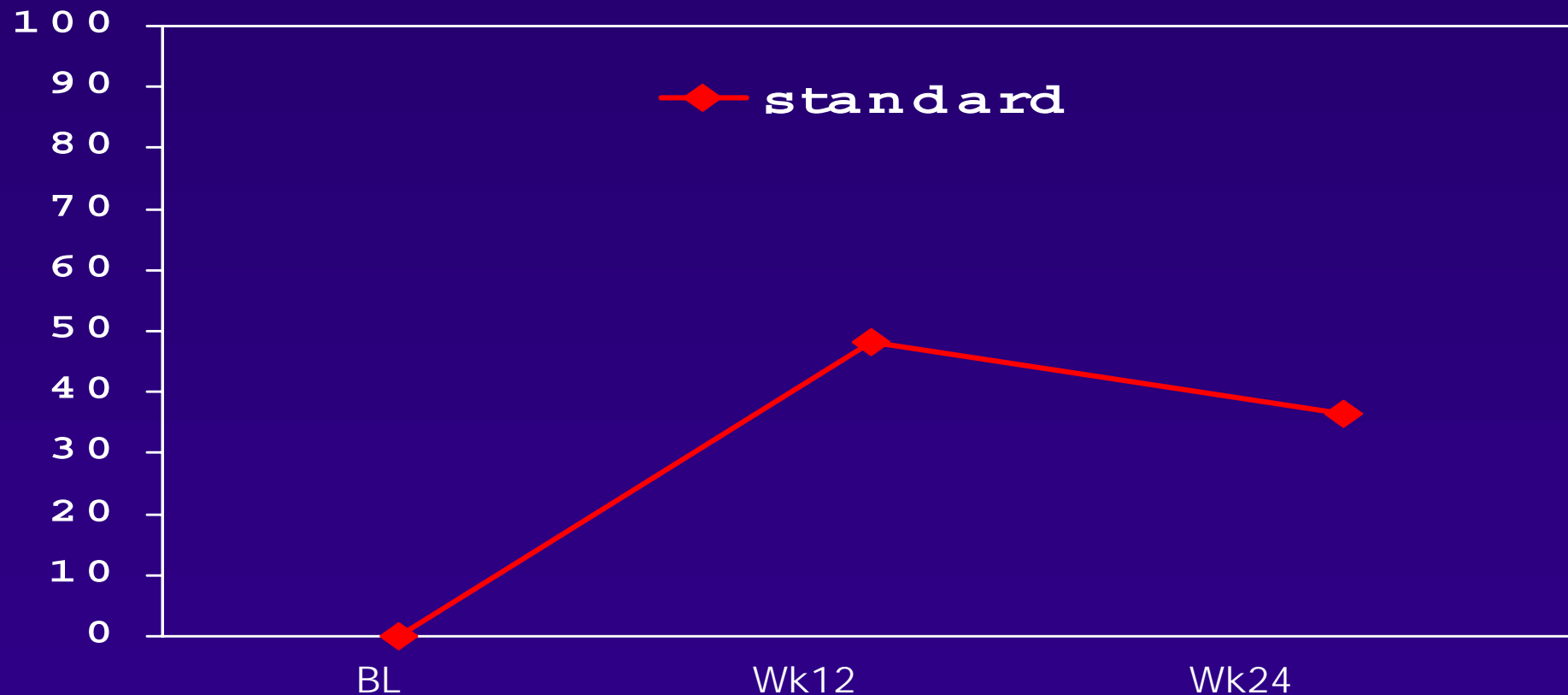
**University Hospital Utrecht**

# Mean change plasma HIV-RNA from baseline at month 3 and 6 in Control and Genotypic arms.



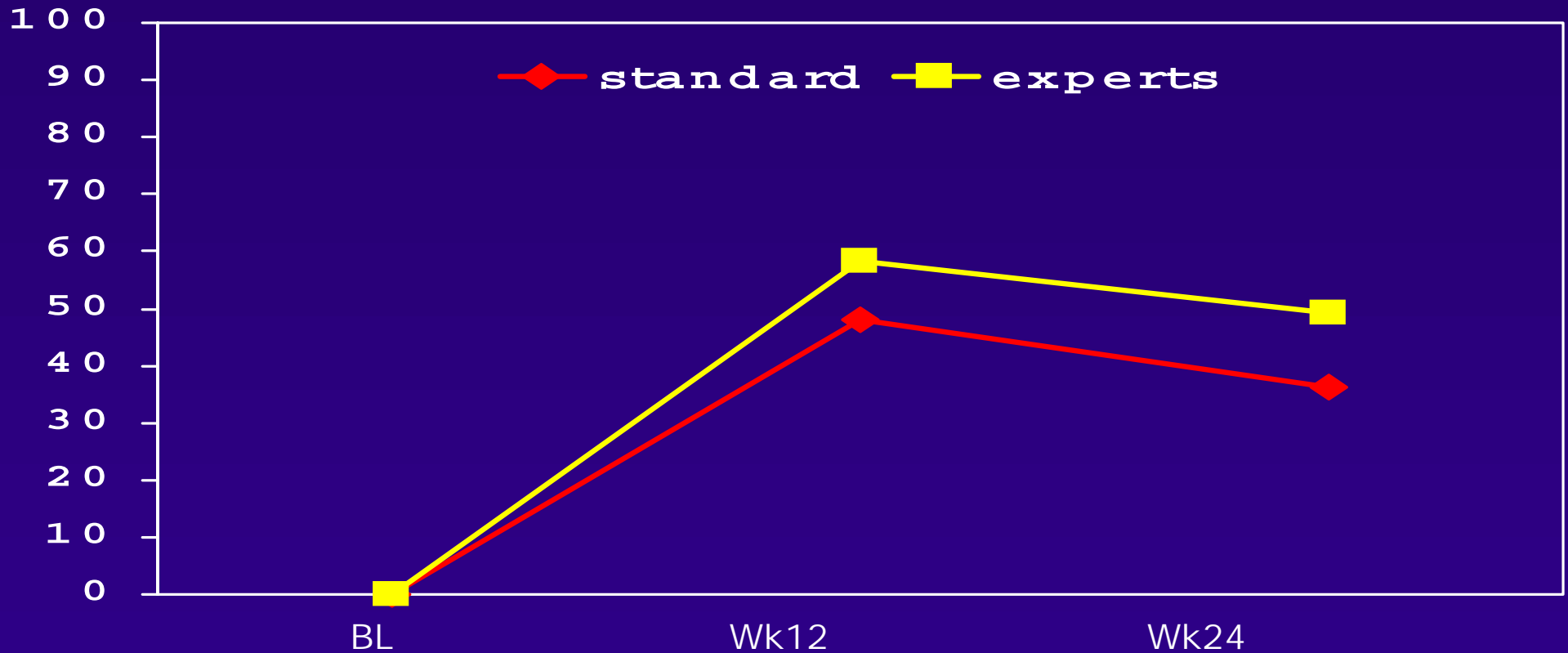
# Results - Havana

% of Patients with HIV-1 RNA <400 copies/ml



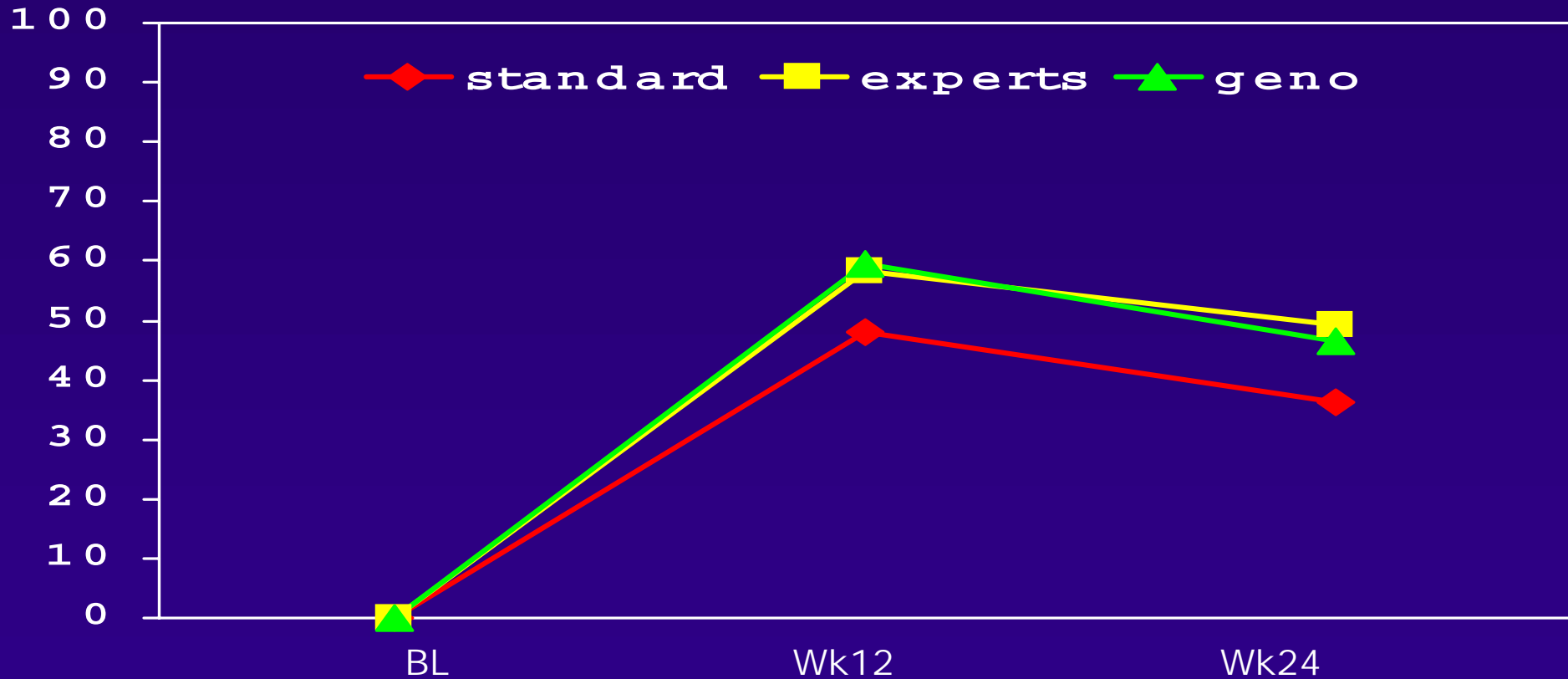
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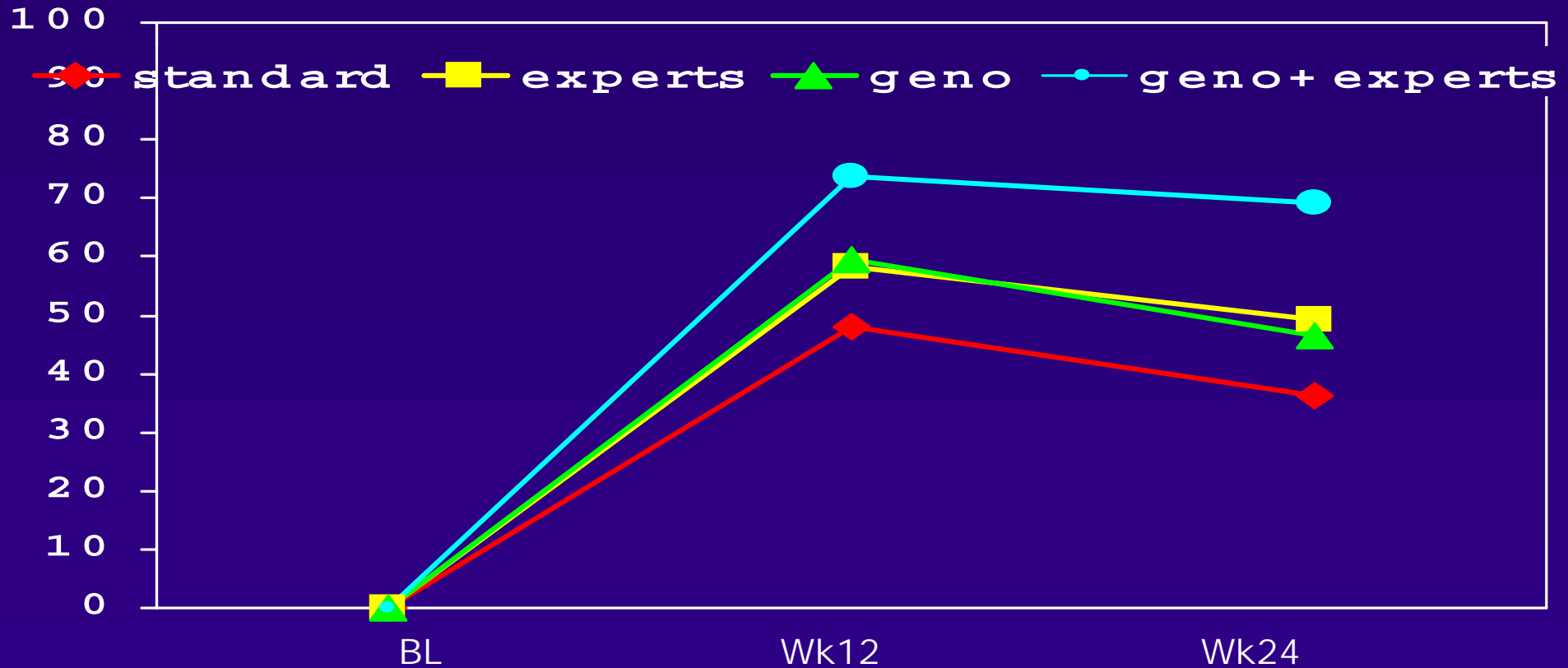
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Three of four randomized studies showed (short term)  
virological benefit for genotyping

Only one out of four prospective phenotyping studies showed a benefit for phenotyping over standard of care.



A proper interpretation of a genotype requires an understanding of the relationship of mutations with phenotype and/or virological outcome.

## Comparison of Interpretation Systems

IS	Predict Success	Predict Failure	Predict Total
Stanford	72.9	70.5	71.8
Geno2Pheno	65.7	67.2	66.4
Retrogram	82.9	72.1	77.9
VGI	71.4	75.4	73.3

Benefits derived from genotyping will depend on interpretation and integration.

All guidelines (USA, Europe) recommend resistance testing (genotyping) for patients failing therapy.

## Cost effectiveness of genotyping (weinstein 2001):

- based on published randomized trials
- in failing patients cost effectiveness similar to many recommended interventions (HAART)

Should we test at baseline?

-primary infection

- chronically infected

Test at baseline?

- resistance transmission

- viral subtypes

- Transmission of drug resistance (all classes) has been reported in Europe
- Virological response to treatment in patients with transmitted resistant virus are compromised.



## Transmission ZDV / 3TC Resistance

	Years	(N)	ZDV (d4T)	3TC	NNRTI
France	96-97	(130)	6%	4%	?
Marseille	95-98	(34)	18%	6%	?
Italy	93-97	(36)	10%	0%	?
England	88-98	(108)	7%	0%	0%
Netherlands	92-96	(52)	11%	?	?
QUEST	98	(82)	7%	4%	13%
Switzerland	96-99	(147)	9%	3%	2%

M. Harzic, C. Tamalet, C. Loveday, D. Pillay, K. Porter, V. Miller, L. Goh, S. Yerly personal communication; C. Riva *UMC* Williams; 2nd International Workshop on HIV Drug Resistance, Lake Maggiore, Italy 1998., J. Goudsmit, Colloque *Virology* CLRS, Lausanne October 1998.

## Viral subtypes

- "Natural" resistance in NNRTI
- Pathways to resistant may be different from subtype B

Nelfinavir treatment

In subtype B follows the D30N pathway

In subtype C follows L90M pathway

Therefore different subtypes failing the same drug may therefore respond differently to their second regimen.

## Baseline resistance testing may benefit:

- Individual patients, better response
- Population, will generate insights into the spread of drug resistant virus
- Provide information on the transmission of the various subtypes and insight into the dynamics of the epidemic

In conclusion, resistance testing (genotyping) should be considered standard of care for patients **failing** therapy, and (potentially) for patients **starting** therapy.