At this presentation we introduce a new challenge to developing a novel treatment for HIV Under Title

the Antibodies of Reverse Transcriptase System. A Novel Approach to Inhibit HIV-1 Infection by actively neutralizing

By

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According to UNAIDS epidemic data 2011, 34 million people are living with HIV, only 25% of them receive treatment, 72% of infected children did not receive any treatment.

The estimated no. of the newly infected people is about 7000 person every day .

The great majority of the infected people are living in sub Saharan AFRICA.

The annual cost of supporting a HIV patient on the current treatment is approximately between 14000and 20000 dollar/year, this for outpatient medical support regardless of the cost of the expenditure analysis needed.

The current medications for HIV patient if he takes them for life time could be well over 400,000 dollar.
2.3 billion $ /year is the expected cost for treating HIV patients all over the world.

In identifying the mechanism by which HIV-1 causes disease two major hypothesis have been forwarded

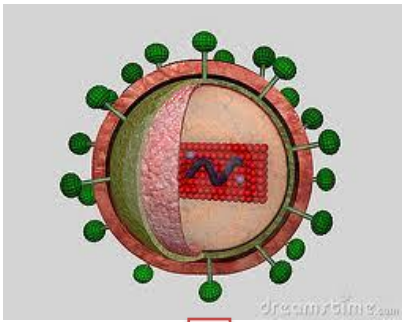
The first hypothesis :

HIV-1 cause loss of CD4 T-lymphocyte by directly infecting and killing these cells.

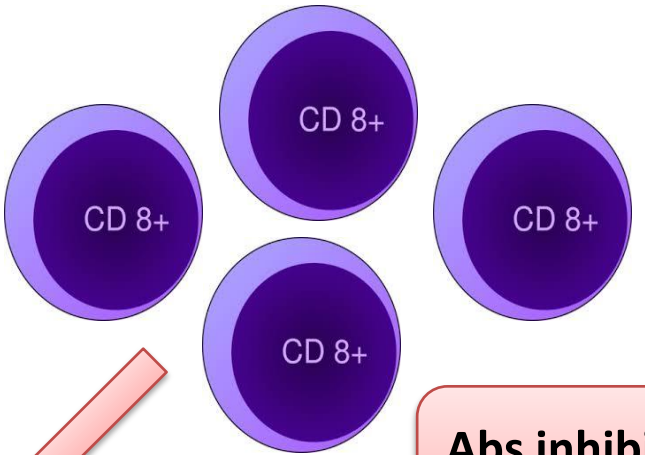
The second

Base on observation that infected and uninfected are affected.

A novel hypothesis for pathophysiology of HIV-1

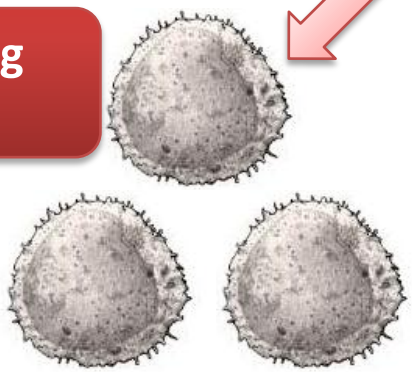


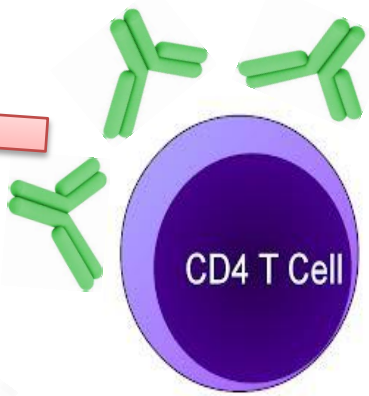
CD8 try to outcome the HIV and exhausted from long standing activation



Abs inhibits the CD4 T- cell

Lyses of CD8 and aging Of CD4 T- cell





HIV-1 stimulate the B-cells

Plasma cells to produce Abs

. The HIV-1 antibodies

is our target

↓

To stop its production

↓

To paving the way for CD4 T-cell

Our combination: VK 25 RD

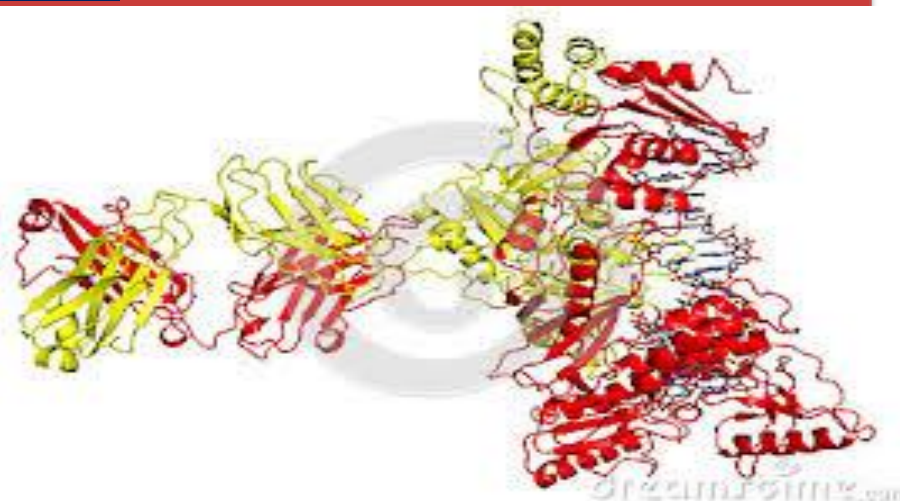
In Vial form 6 ml a liquid pharmaceutical compositions comprise 120 units of both

1-AMV RT (Avian Myeloblastosis Virus)

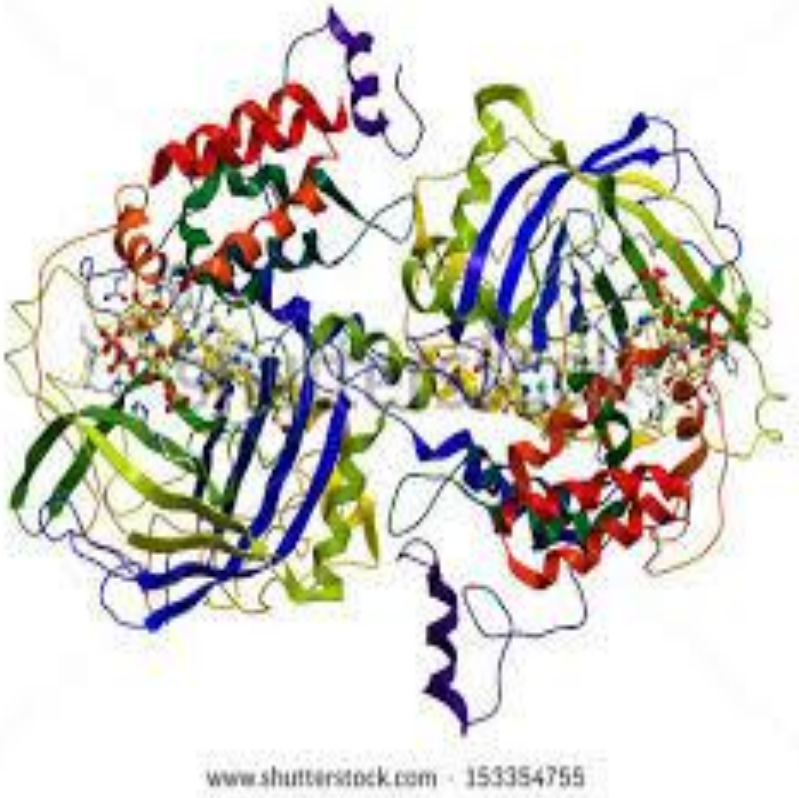
2-DNA polymerase

in specific acceptable pharmaceutical organic solvent

1-RT HIV-1 enzyme is an essential part of the virus.



2- DNA, polymerases



Why we use these components ?

1- Generation of cross reactive antibodies to inhibit the reverse transcriptase (RT) of human immunodeficiency virus type-1(HIV-1)

Novel role for DNA polymerases In immune cells remodeling and regulation.

1-Materials and Methods

10 patients (3 female and 8 male) were eligible for inclusion in this study if they were between 5-40 years

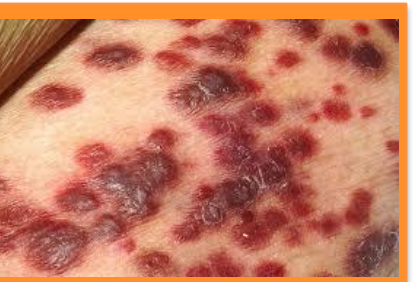
- Five patients take the treatment

  [Test group]

- Five who participated in the study by blood samples donates only

  [Control group]

Patient's inclusion criteria



1-All were positive for HIV antibodies and confirmed by (HIV-RNA-PCR)
2-having signs and symptoms of HIV. (Mild fever, weight loss, diarrhea, lymphadenopathy and opportunistic infections
3-were never having been treated with any antiretroviral drugs

Study site

- This study applied between October 2011 and February 2014 in R & D center, (as a private center).

. All of them consented to take the therapy in the form of S/C injection two times daily for 24 weeks.

- **<u>Consent for participation to taking a novel treatment for HIV</u>.**

- **This treatment under trails, not approved**
- **The preclinical studies for this treatment (Toxicological study) are very save and there is no any unexpected side effects had been recorded.**

- **I consent voluntarily to participate as a participant in this research, having the right that to withdraw from the research at any time without in any way affecting my medical care. I have read the foregoing information, or it has been read to me. I have had the opportunity to ask questions about it and any questions that I have asked have been answered for my satisfaction.**
-

- **Name of Participant_____**
-
- **Signature of Participant _____**
-
- **Date _____**
-
- **Day/month/year**

Exclusion criteria

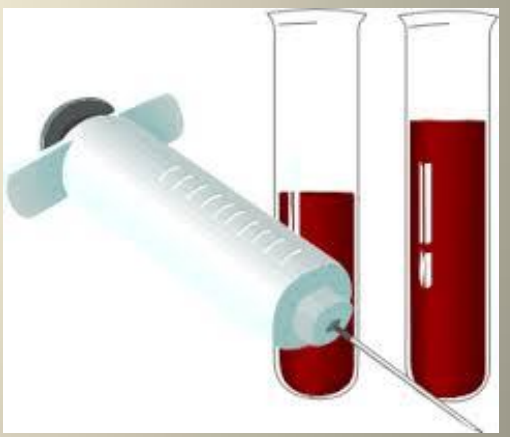
- Patients were excluded if they had any chronic diseases (Diabetes, renal & liver affection, hypertension, cancer) or Hepatitis viral infection (HCV & HBV)

Injectable material

- In Vial form 6 ml liquid pharmaceutical compositions

Serological testing

- Ten blood samples were collected before the treatment and at week 6,12,18,24 from both groups and examined for the following **Immunological tests**
- Quantitative HIV-PCR,
- CD4 count
- HIV antibody
- Anti –RT AMV antibodies



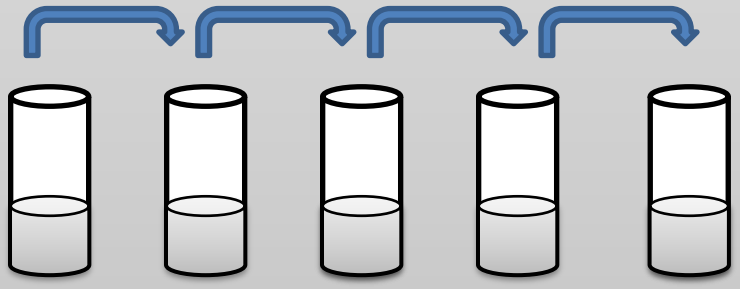
The aim of our trails

1-1 Detection of (Anti-RT AMV) monoclonal antibodies.

This test to prove that serum samples of all treated patients with the novel therapy formed anti-RT AMV Abs

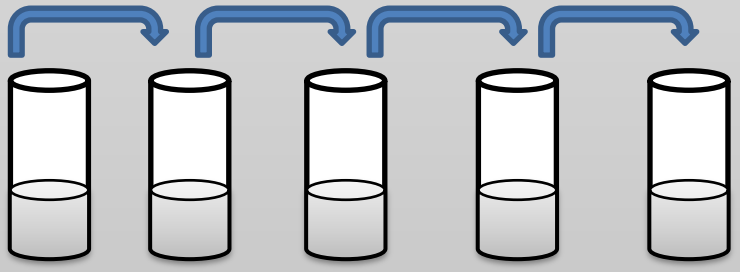
Test group

Serum sample

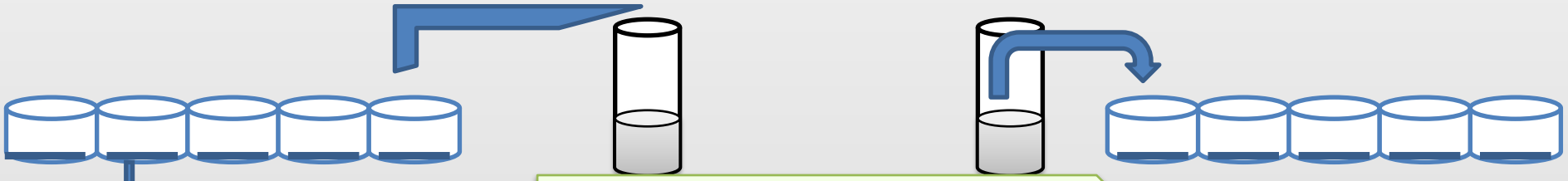


Control group

Serum sample



Serial dilution was made0.2,0.4,0.8,1.6 and 3.2 for every serum sample of both groups at week 6,12,18 and 24.



Elisa wells was coated with 1 ug/ml RT-AMV

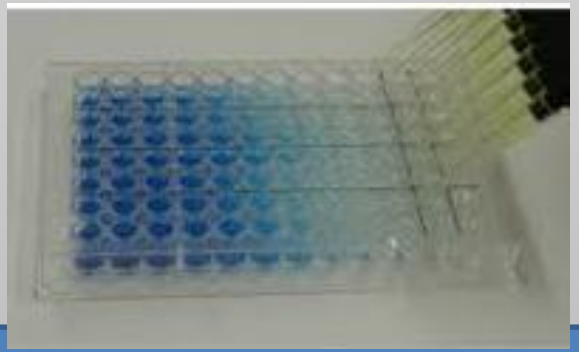
100 u from every dilution was added to coated well

To allow for Ag & Abs reaction

Conjugate was added

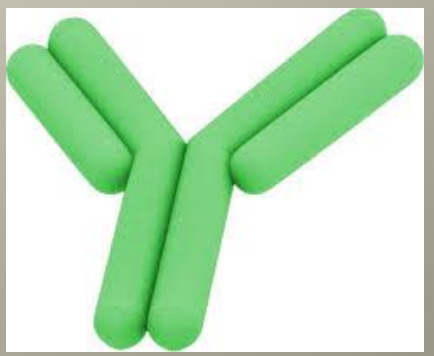
Addition of substrate

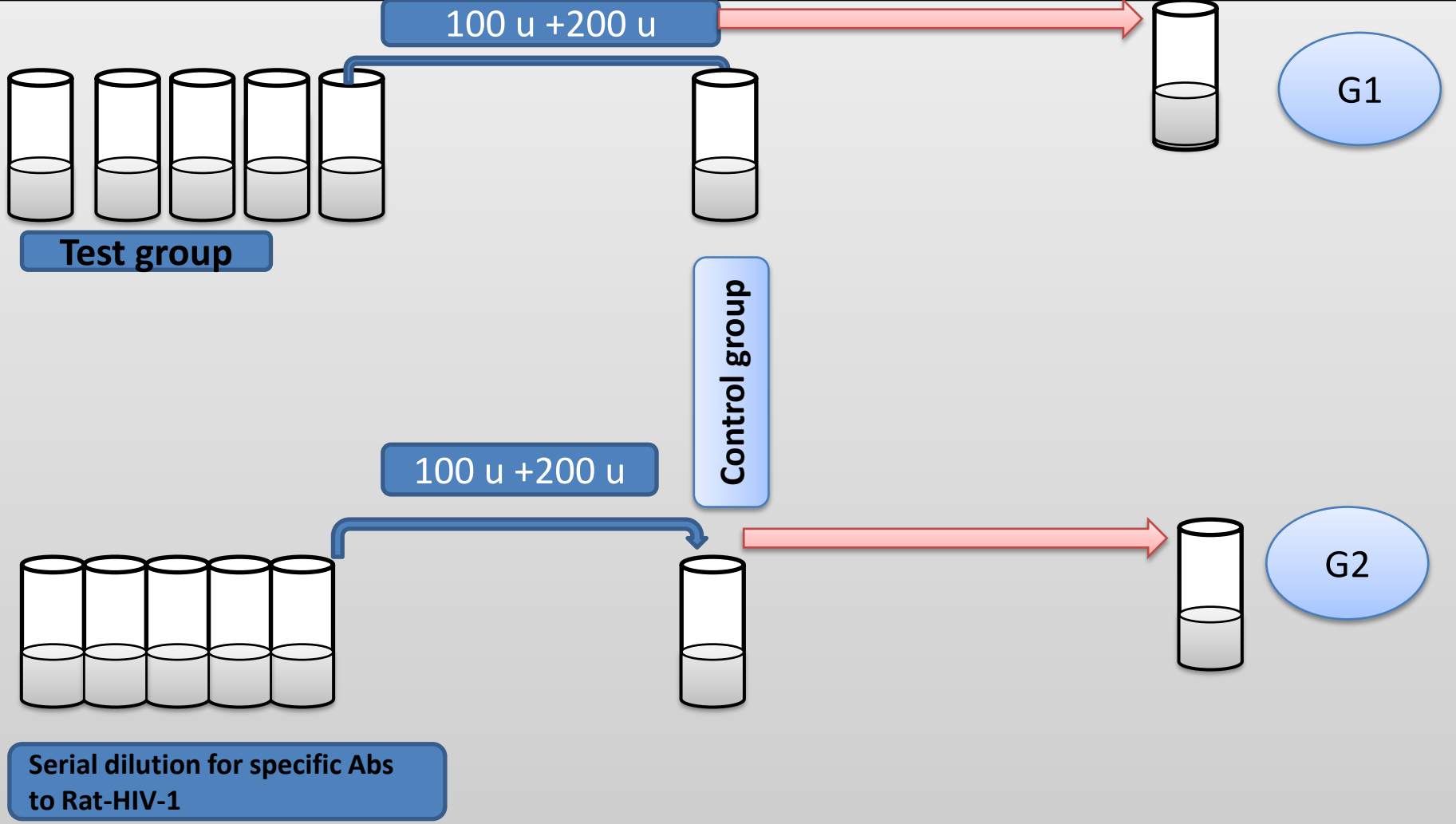
Reading the wells with autoreader



Detection of Anti-RT AMV Antibodies in serum diluted samples of both groups

1-2 Determine the inhibitor effect of Anti-RT AMV on RT HIV-1 biological activity





1-2 Determine the inhibitor effect of Anti-Rt AMV on RT HIV-1 biological activity

To confirm that:

1- serum samples of test group has an anti-RT Abs to AMV-RT .

2- This Abs has the ability to bind the RT-HIV-1 by cross reactivity and can stop it's biological activity.

3-also to confirm that specific anti-RT HIV-1 has not able to stop the HIV-1 RT in serum sample of control group that not treated with the novel therapy.

Results

- We collected the results of all immunological data before starting the treatment regimen and during week 6, 12, 18 and 24 to comparing the difference .

It showed surprisingly

A- undetectable viremia

(reference range < 16 copies/ml).

B- significant elevation in

CD4+ T-lymphocytes above 500 cells/ml .

C- HIV antibodies by enzyme-linked immunosorbent assay (ELISA) testing were negatives for about 4 patients from 5.

Patients clinical presentation:

The patients reported a significant improvement of their clinical picture, and the constitutional symptoms of HIV infection (AIDS):

No diarrhea , disappearance of muscle ache and opportunistic infection, weight gain and no notable lymph nodes beside marked improvement of the psychological conditions

1-1 serological test reports

For formation of neutralizing mAbs to AMV RT enzyme during week 6, 12, 18 and 24.

Fig 1. Show the increasing in the concentration level of neutralizing Abs at 12, 18 and marked decrease in his level at 24, 48

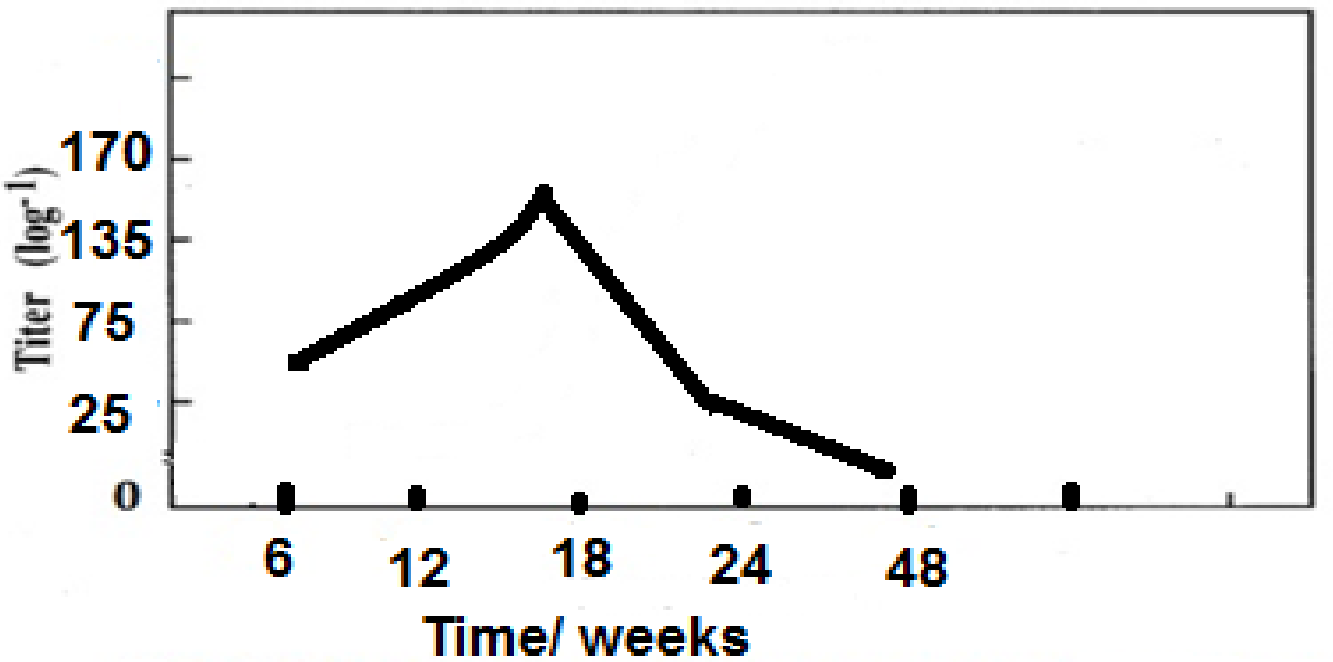


Fig 1.showed the highest concentration level of IgG AMV-RT neutralization Abs during week 12, 18 and marked decrease in conc. at 24 weeks

Successful test of the hypothesis

Comparing the results of (HIV-RNA-PCR),

- **Of** test group (G 2)
- Specific mAbs to HIV-1 RT Sample(G 1)

Follow up: after 48 weeks

All volunteers are physically and psychologically good and their immunological data still give below detection limits by HIV-1 RNA –PCR,HIV-1 Abs negative and CD4 T-cell over 600 cells/µL

Table 1. immunological tests for all patients before treatment. (Test group include patients from (X1-X5) (Control group from X6- X10)

parameters	X1	X2	X3	X4	X5	X6	X7	X8	X9	X10
CD4	270	315	180	170	150	340	303	178	349	213
PCR	92.000	105.000	470.000	4300	315.000	367.000	4.000	34.000	1.900	24.000
HIV Ab	+ve	+ve	+ve	+ve	+ve	+ve	+ve	+ve	+ve	+ve
Wt	67	62	79	77	71	58	64	67	28	25

Table 2. 6 weeks after the beginning of the treatment.

parameters	X1	X2	X3	X4	X5	X6	X7	X8	X9	X10
CD4	430	400	455	670	340	430	290	201	231	240
PCR	2300	-ve	4000	-ve	32.000	210.000	1.200	18.000	-ve	6.000
HIV Ab	+ve	+ve	+ve	+ve	+ve	+ve	+ve	+ve	+ve	+ve
Wt	66	66	78	70	70	56	62.4	61	27	24

Table 3. 12 weeks after the beginning of the treatment

.

parameters	X1	X2	X3	X4	X5	X6	X7	X8	X9	X10
CD4	570	560	600	650	800	390	460	210	223	255
PCR	-ve	4.000	-ve	-ve	-ve	128.000	-ve	2000	-ve	450
HIV Ab	+ve	+ve	+ve	+ve	+ve	+ve	+ve	+ve	+ve	+ve
Wt	71	64.5	83	70.4	73	55	65	59	26.3	25.7

Table 4: After18 weeks from the beginning of treatment, these tests are done for all patients,

Parameters	X1	X2	X3	X4	X5	X6	X7	X8	X9	X10
CD4	540	530	780	610	670	500	340	190	240	310
PCR	-ve	-ve	-ve	1.620	1.300	12.000	-ve	-ve	-ve	-ve
HIV Ab	+ve	-ve	-ve	+ve	+ve	+ve	+ve	+ve	+ve	+ve
Wt	73	65	82	71	71	58	63	58	25	23

Table 5: 24 weeks from the beginning of the treatment.

Parameters	X1	X2	X3	X4	X5	X6	X7	X8	X9	X10
CD4	810	670	760	665	700	278	300	300	320	400
PCR	-ve	-ve	-ve	-ve	-ve	-ve	-ve	-ve	-ve	-ve
HIV Ab	-ve	-ve	-ve	Equivocal	Slightly +ve	+ve	+ve	+ve	+ve	+ve
Wt	73	64	82.2	70.2	68	55	62	60.5	23	25
CD4 normal range:350-500 cells/µL										

Conclusion

Recent Treatment:

The recent trend of treating HIV/AIDS is to combine at least three drugs from two different classes , these classes include :

1- non-nucleoside reverse transcriptase inhibitors (NNRTIs)

2-nucleoside reverse transcriptase inhibitors (NRTIs), protease inhibitors (PIs),

3-fusion inhibitors and integrase inhibitor .

The side effects of these drugs are remarkable. They never lead to complete cure whatever the time they take but they aim to

- ameliorate the clinical picture,
- increase CD4 cell count
- decrease the viral load.

But when we Stop the treatment

the HIV-1 spread again and more CD4 T-cell infections.

. At the present time there is a need for new drugs .

- **The results described in this study support our hypothesis.**

- This study introduces a new strategy for HIV (AIDS) cure differing from all conventional methods .

.Our medication (VK 25 RD)

once become available

- it will be a promising
- life saving drug

this is a world dream for the last three decades

- So we emphasize that a further extended and tedious study is needed to evaluate the
- benefits and values of the compound

Thank you