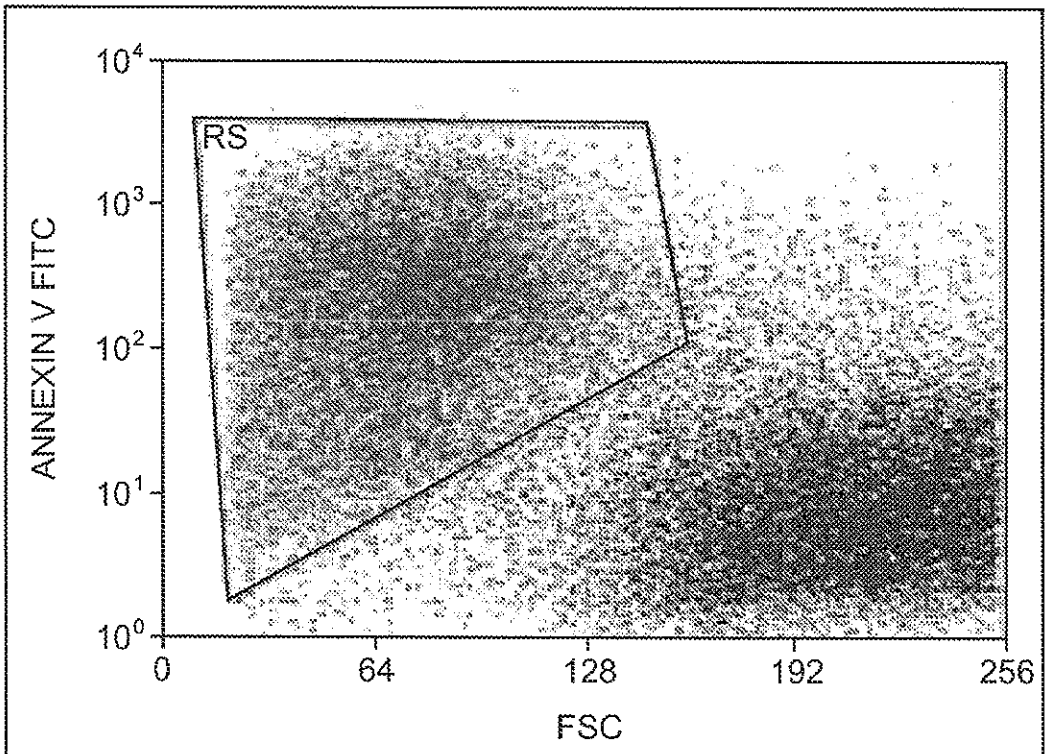


Regon	Count	%	Mean	CV
Total	49400	100.00	141.00, 179.62	49.75, 206.04
RS	22243	45.02	74.48, 361.18	39.70, 130.00

FIG. 1

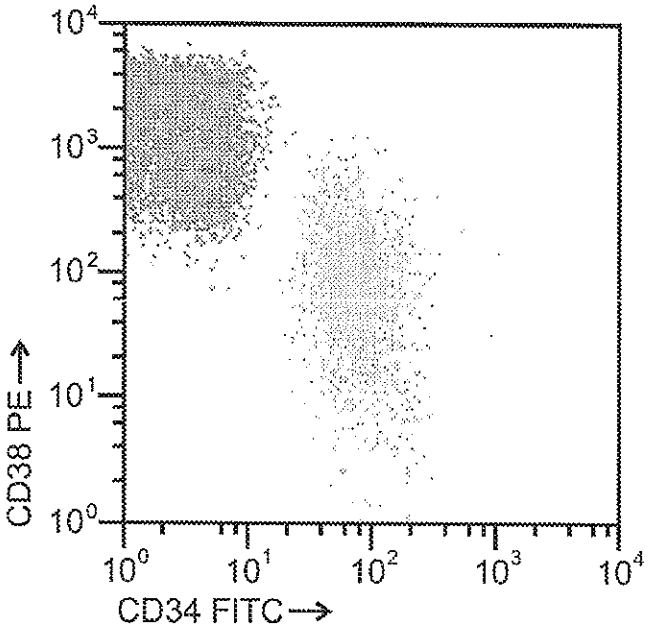


FIG. 2

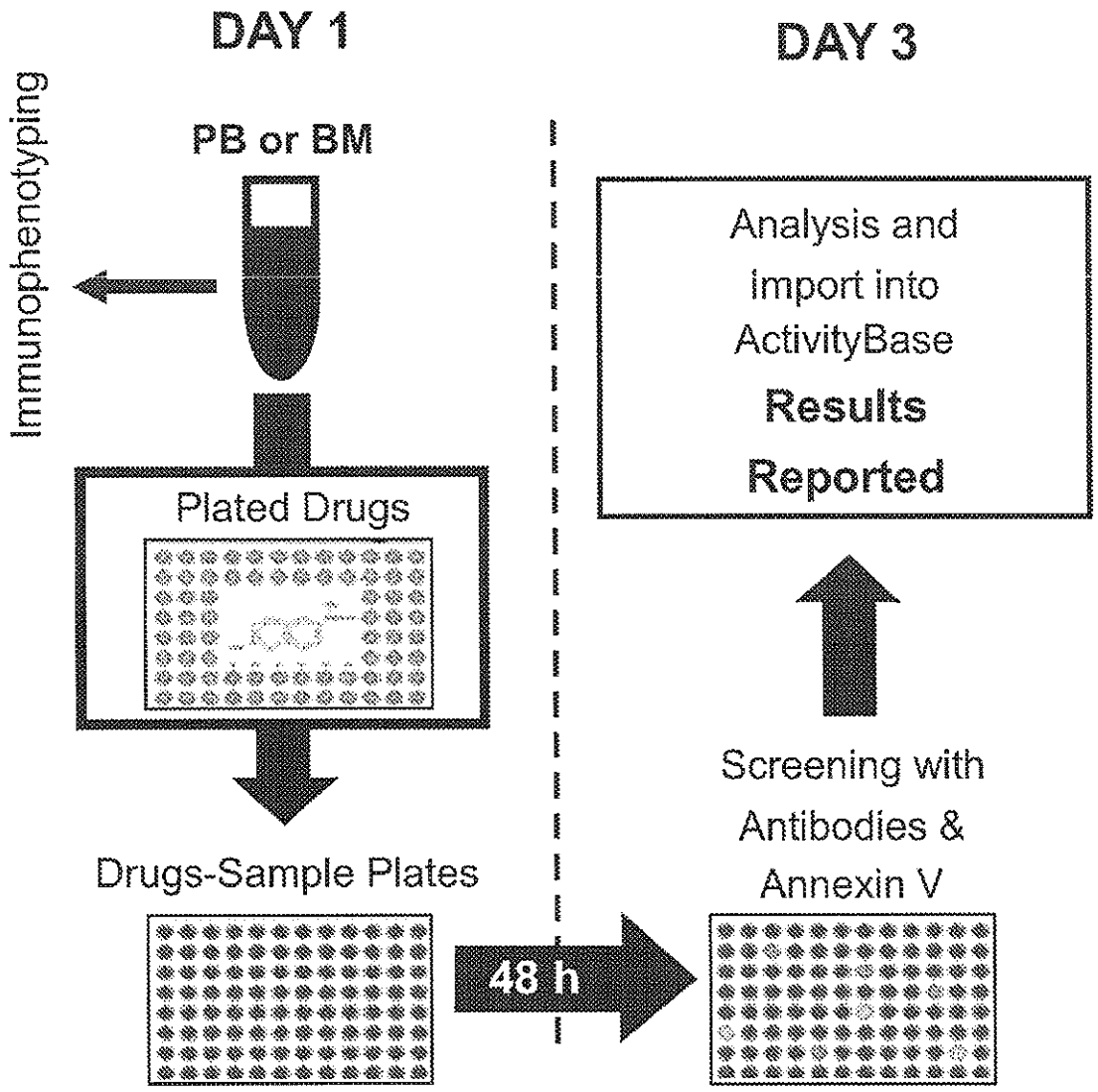

DAY 1
DAY 3
Immunophenotyping
PB or BM
Plated Drugs
Drugs-Sample Plates
48 h
Analysis and
Import into
ActivityBase
Results
Reported
Screening with
Antibodies &
Annexin V

FIG. 3

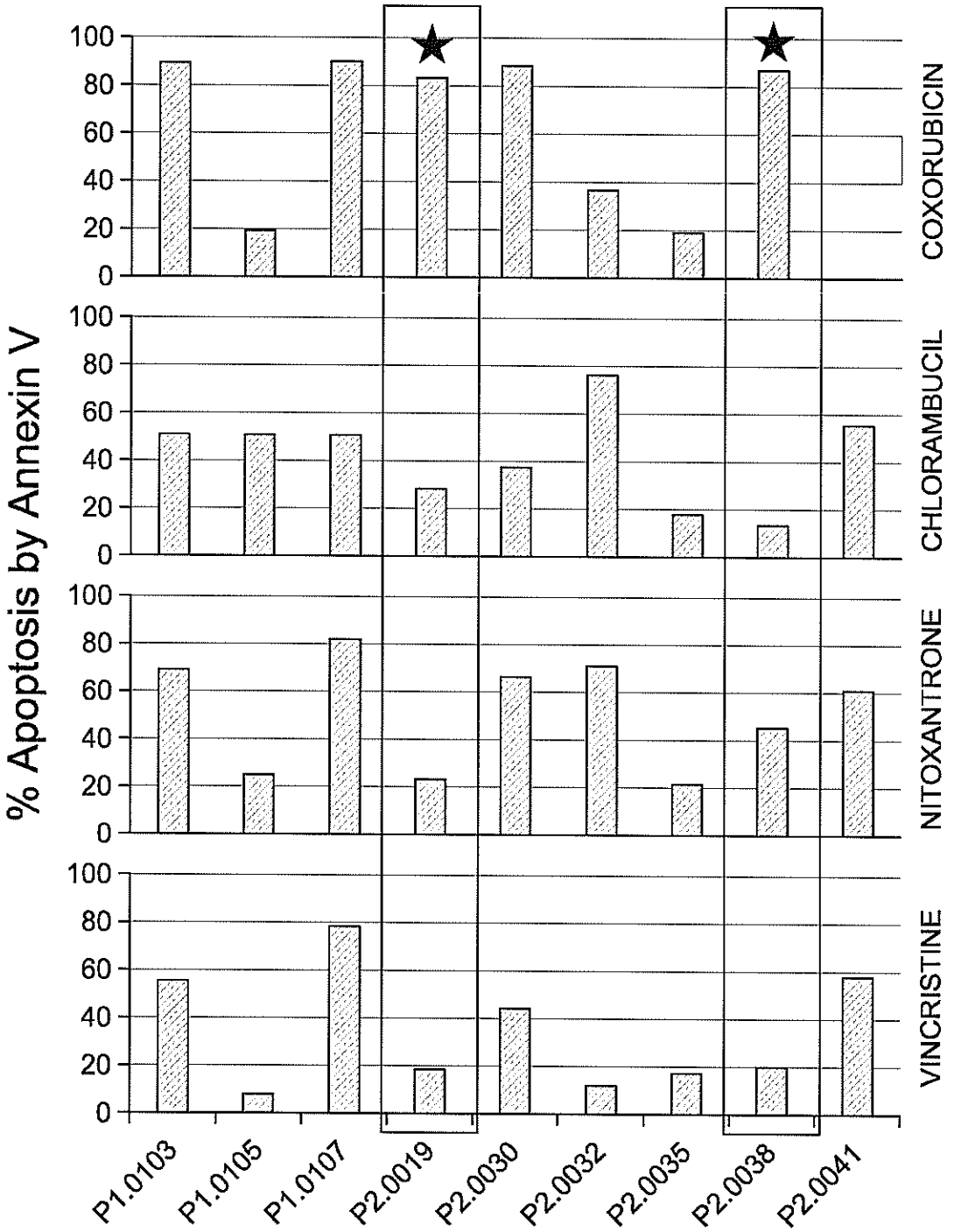

% Apoptosis by Annexin V
100
80
60
40
20
0
COXORUBICIN
CHLORAMBUCIL
NITOXANTRONE
VINCRISTINE
P1.0103
P1.0105
P1.0107
P2.0019
P2.0030
P2.0032
P2.0035
P2.0038
P2.0041

FIG. 4

# of Drugs	# of Combinations (of up to 4 drugs)	5 Concentrations	2 incubation times
1	1	5	10
2	3	15	30
3	7	35	70
4	15	75	150
5	30	150	300
6	57	315	630
7	106	635	1270
8	199	995	1990
9	255	1275	2700
10	385	1925	3700
11	561	2805	5610
12	795	3975	7950
13	1092	5460	10920
14	1470	7350	14700
15	1940	9700	19400

FIG. 5

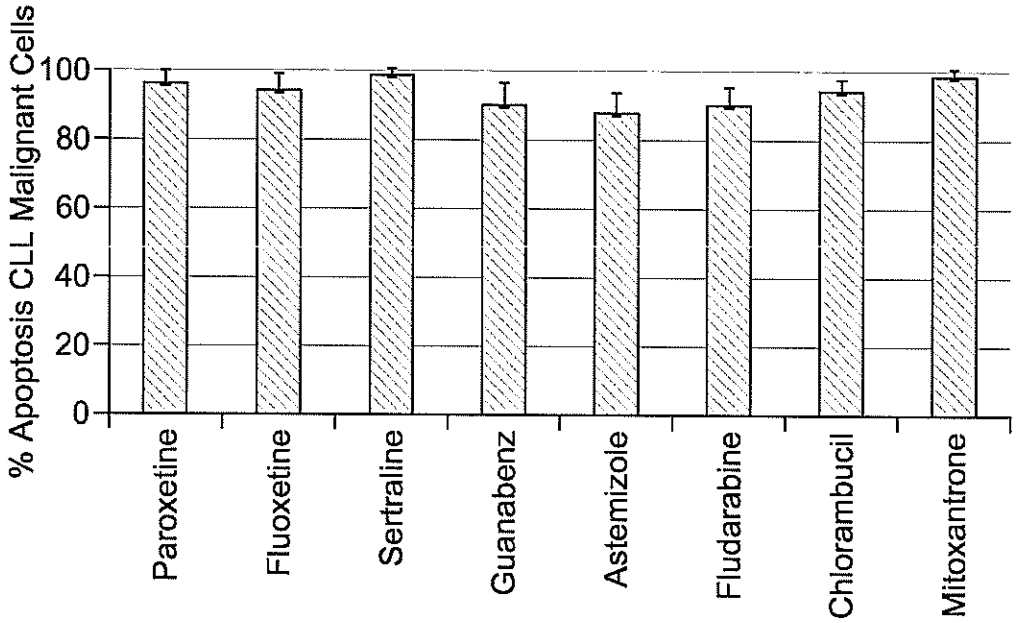

% Apoptosis CLL Malignant Cells
100
80
60
40
20
0
Paroxetine
Fluoxetine
Sertraline
Guanabenz
Astemizole
Fludarabine
Chlorambucil
Mitoxantrone

FIG. 6

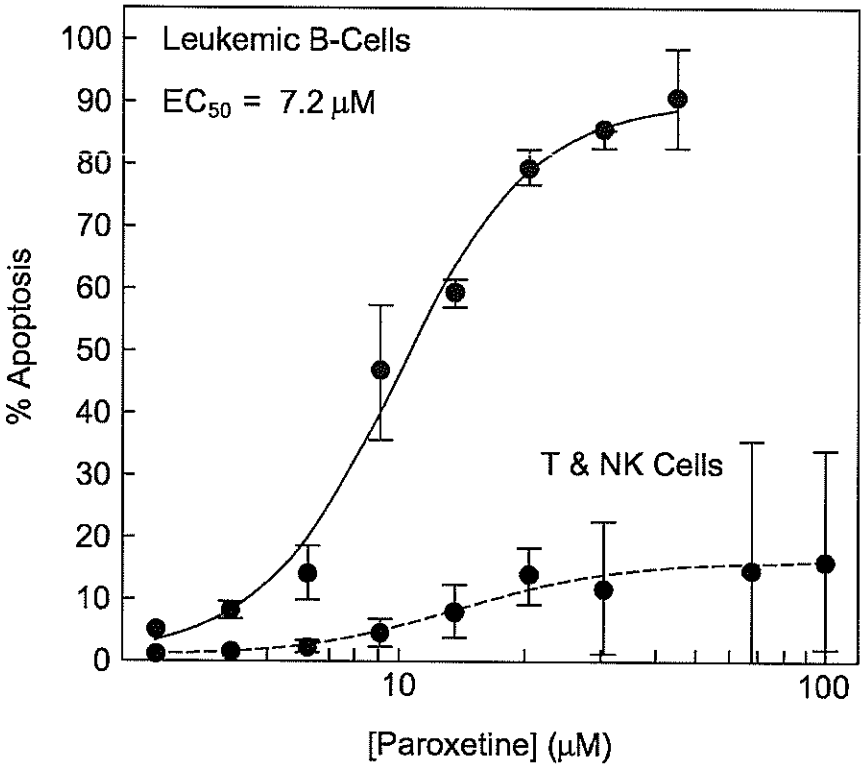

Leukemic B-Cells
EC50 = 7.2 µM
T & NK Cells
% Apoptosis
100
90
80
70
60
50
40
30
20
10
0
10
100
[Paroxetine] (µM)

FIG. 7

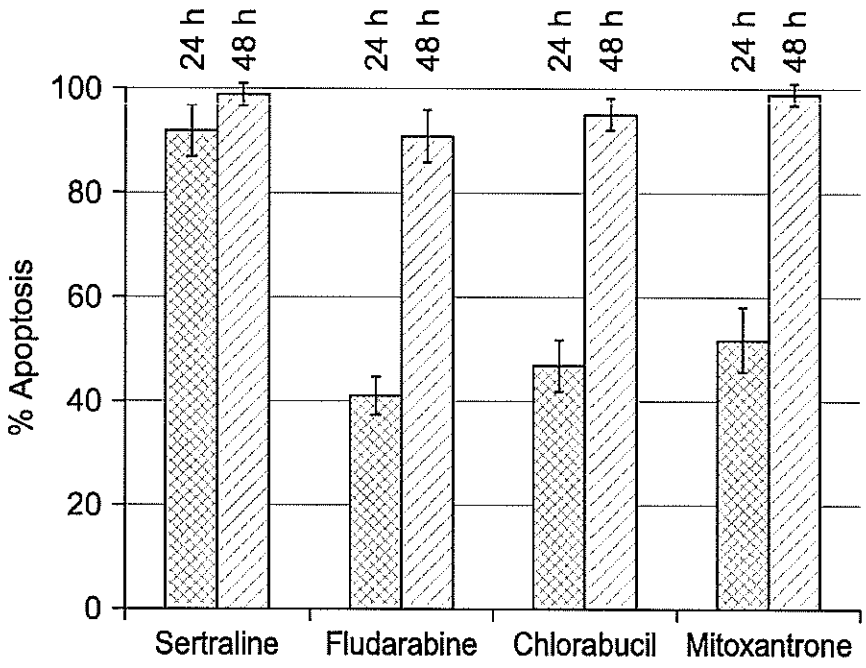

24 h
48 h
24 h
48 h
24 h
48 h
24 h
48 h
100
80
60
40
20
0
% Apoptosis
Sertraline
Fludarabine
Chlorabucil
Mitoxantrone

FIG. 8

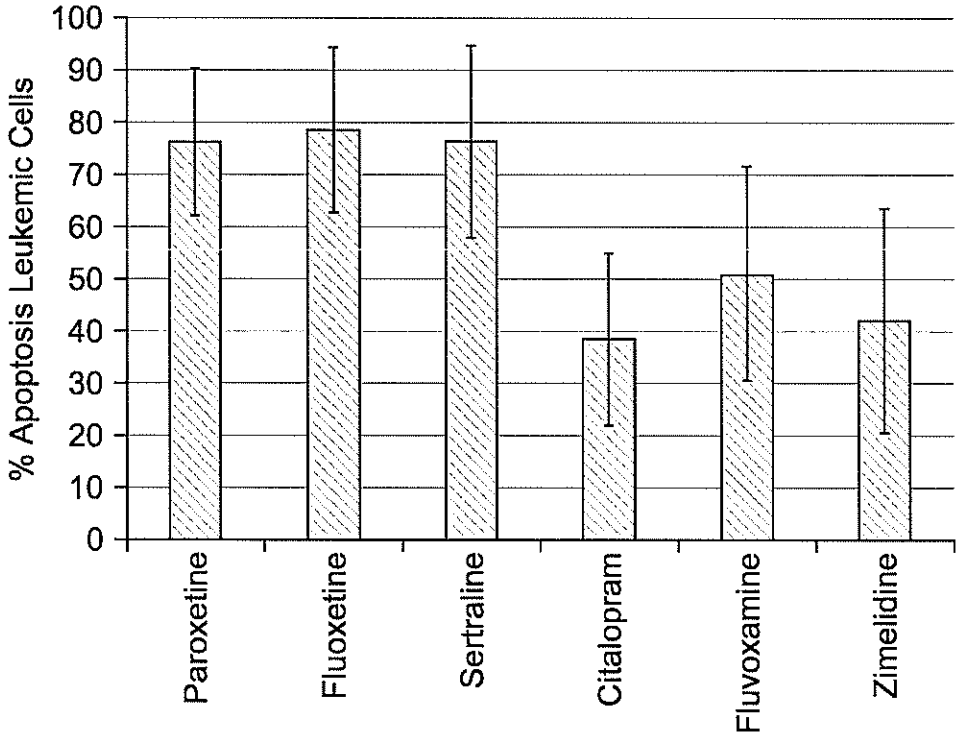

% Apoptosis Leukemic Cells
100
90
80
70
60
50
40
30
20
10
0
Paroxetine
Fluoxetine
Sertraline
Citalopram
Fluvoxamine
Zimelidine

FIG. 9

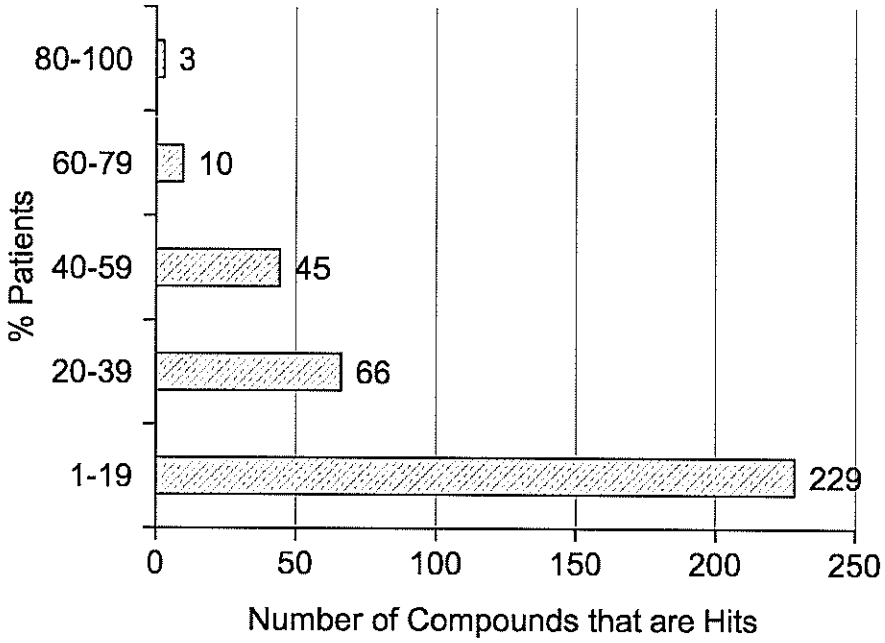

80-100
3
60-79
10
40-59
45
20-39
66
1-19
229
% Patients
0
50
100
150
200
250
Number of Compounds that are Hits

FIG. 10

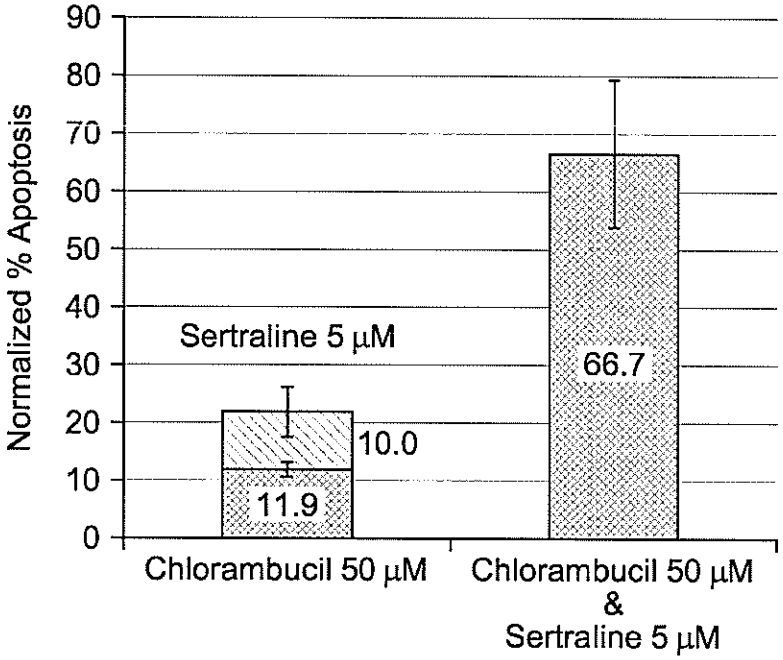

90
80
70
60
50
40
30
20
10
0
Normalized % Apoptosis
Sertraline 5 μM
10.0
11.9
66.7
Chlorambucil 50 μM
Chlorambucil 50 μM
&
Sertraline 5 μM

FIG. 11

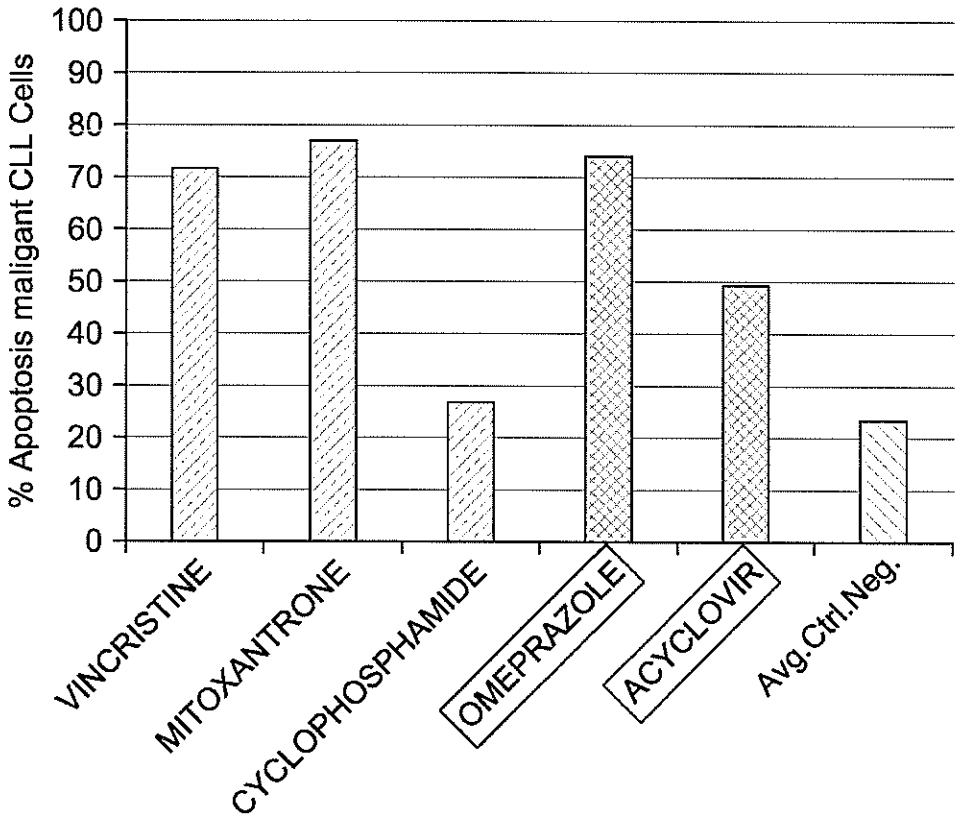

% Apoptosis maligant CLL Cells
100
90
80
70
60
50
40
30
20
10
0
VINCRISTINE
MITOXANTRONE
CYCLOPHOSPHAMIDE
OMEPRAZOLE
ACYCLOVIR
Avg.Ctrl.Neg.

FIG. 12

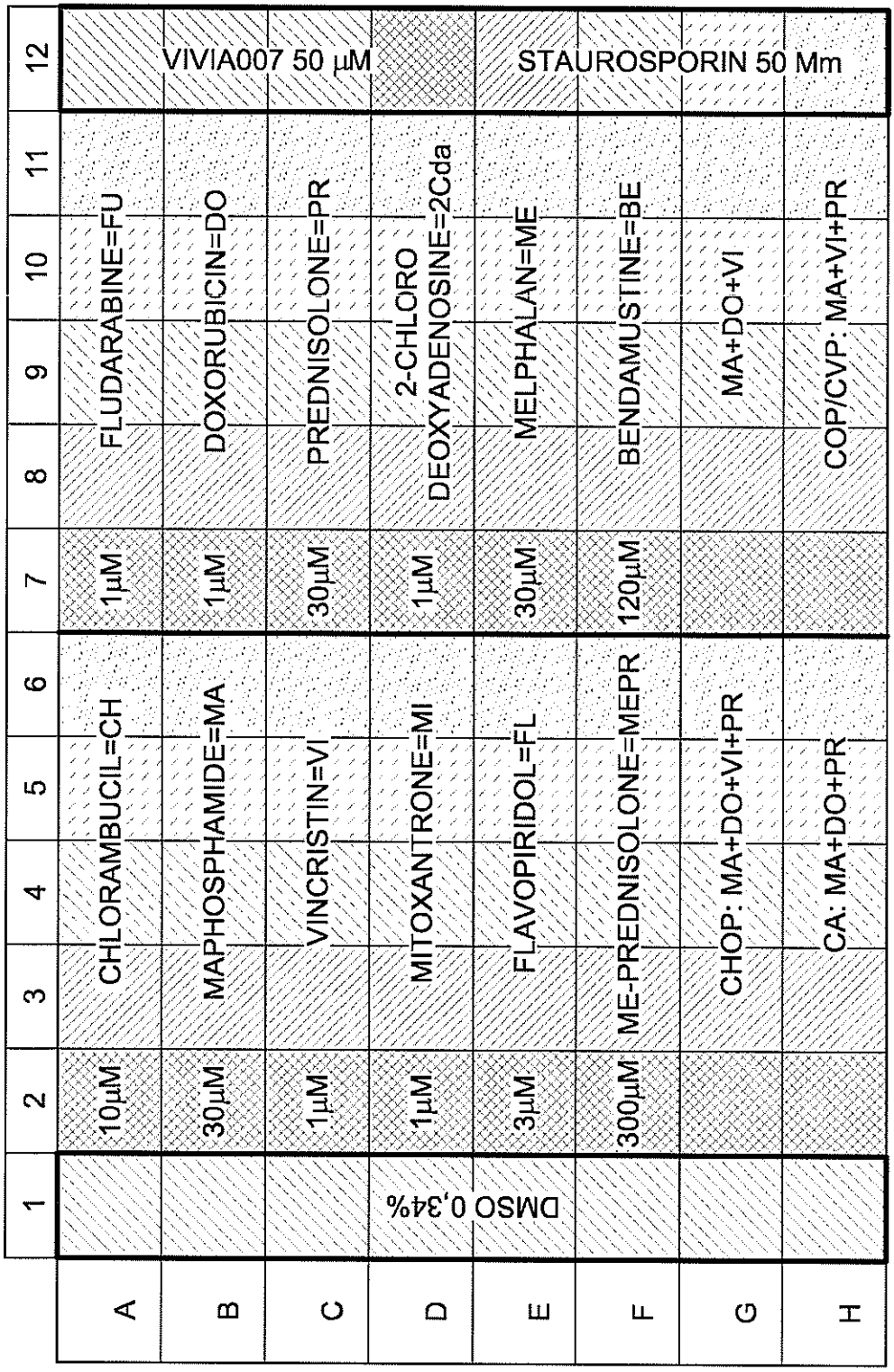

1 2 3 4 5 6 7 8 9 10 11 12
A
B
C
D
E
F
G
H
DMSO 0,34%
10µM
30µM
1µM
1µM
3µM
300µM
CHLORAMBUCIL=CH
MAPHOSPHAMIDE=MA
VINCRISTIN=VI
MITOXANTRONE=MI
FLAVOPIRIDOL=FL
ME-PREDNISOLONE=MEPR
CHOP: MA+DO+VI+PR
CA: MA+DO+PR
1µM
1µM
30µM
1µM
30µM
120µM
FLUDARABINE=FU
DOXORUBICIN=DO
PREDNISOLONE=PR
2-CHLORO DEOXYADENOSINE=2Cda
MELPHALAN=ME
BENDAMUSTINE=BE
MA+DO+VI
COP/CVP: MA+VI+PR
VIVIA007 50 µM
STAUROSPORIN 50 Mm

FIG. 13A

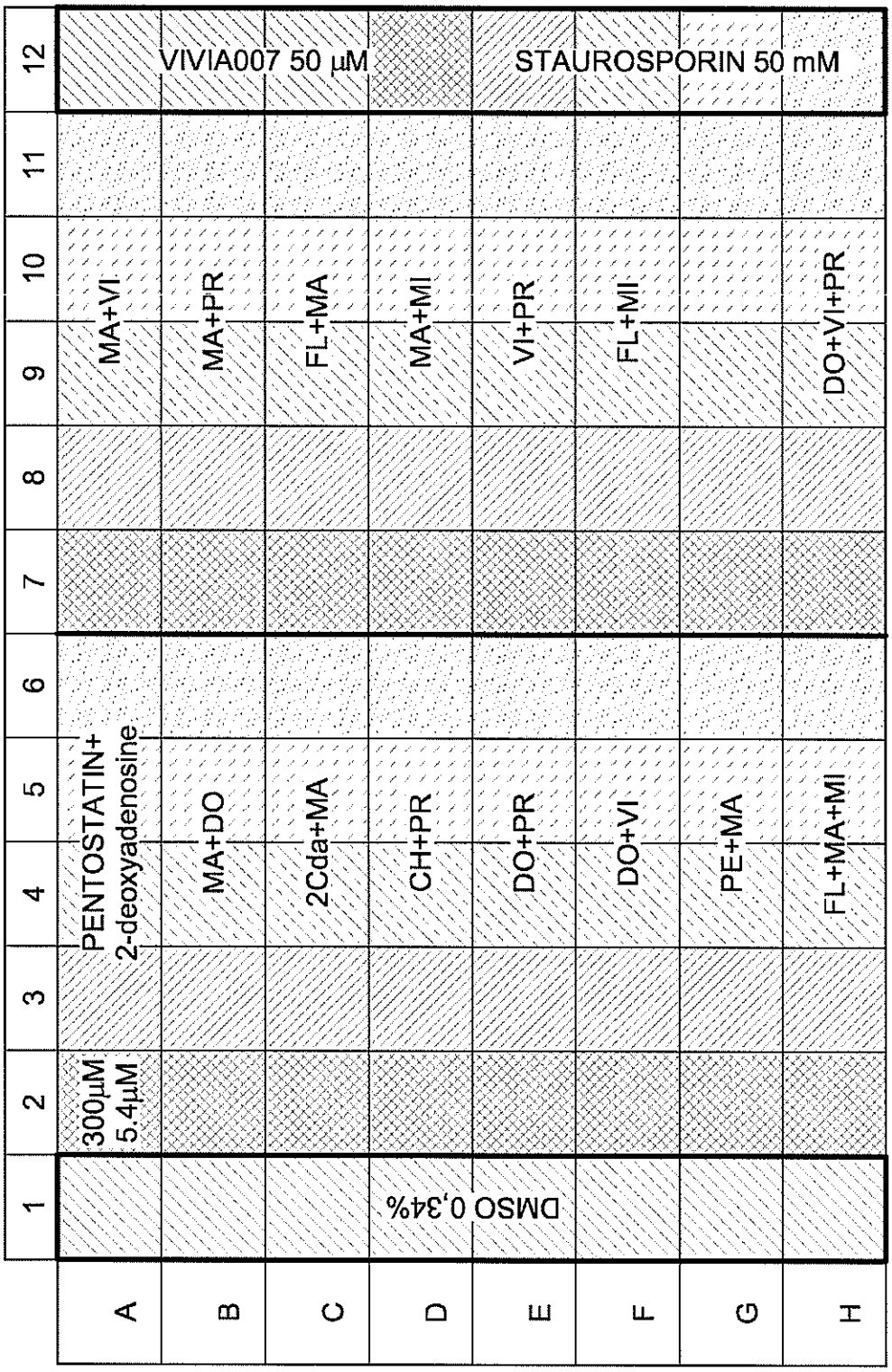

1
2
3
4
5
6
7
8
9
10
11
12
A
B
C
D
E
F
G
H
300µM
5.4µM
PENTOSTATIN+
2-deoxyadenosine
MA+VI
DMSO 0,34%
VIVIA007 50 µM
STAUROSPORIN 50 mM
MA+DO
MA+PR
2Cda+MA
FL+MA
CH+PR
MA+MI
DO+PR
VI+PR
DO+VI
FL+MI
PE+MA
FL+MA+MI
DO+VI+PR

FIG. 13B

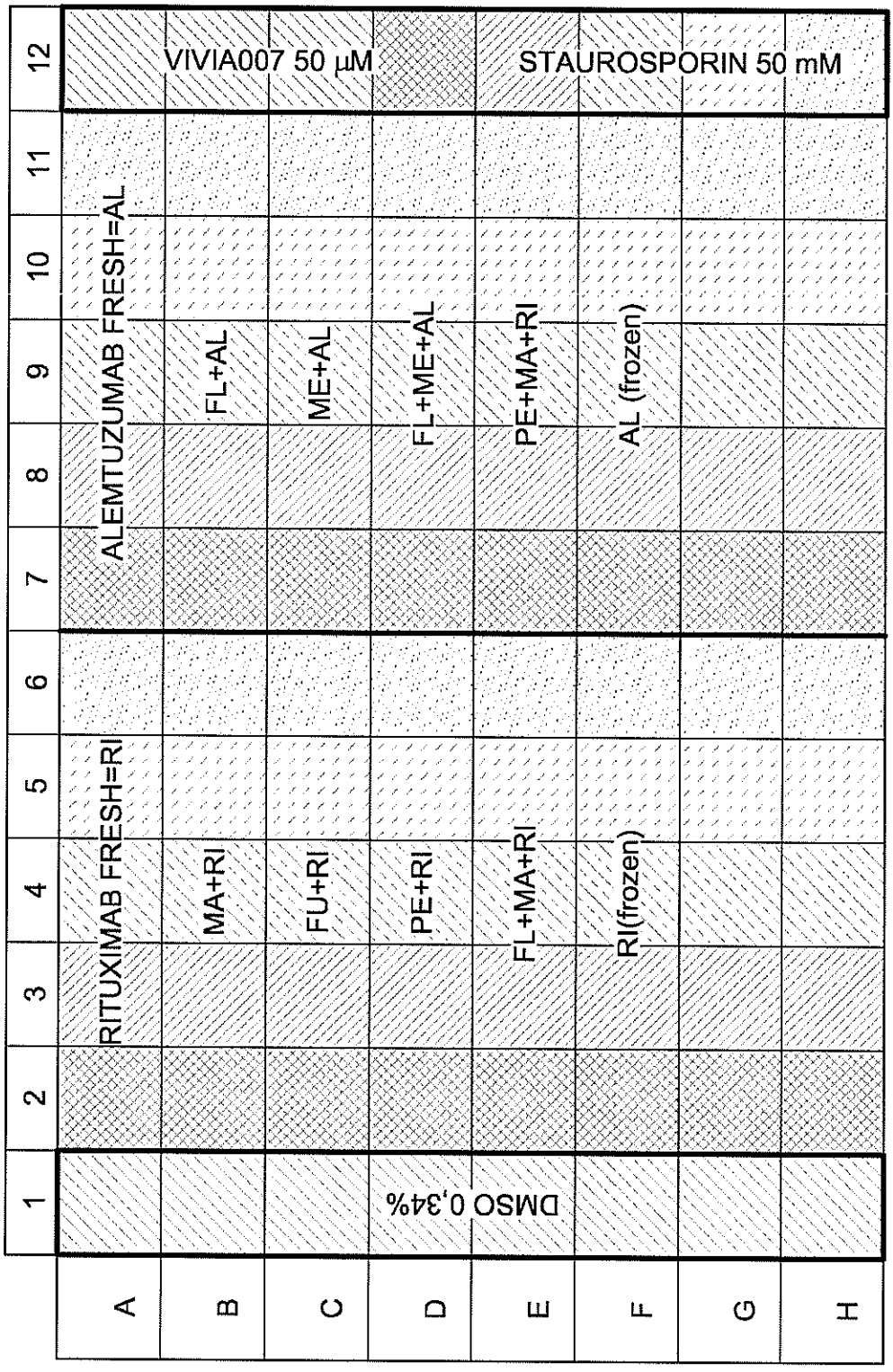

1
2
3
4
5
6
7
8
9
10
11
12
A
B
C
D
E
F
G
H
DMSO 0,34%
VIVIA007 50 µM
STAUROSPORIN 50 mM
RITUXIMAB FRESH=RI
ALEMTUZUMAB FRESH=AL
MA+RI
FU+RI
PE+RI
FL+MA+RI
RI(frozen)
FL+AL
ME+AL
FL+ME+AL
PE+MA+RI
AL (frozen)

FIG. 13C

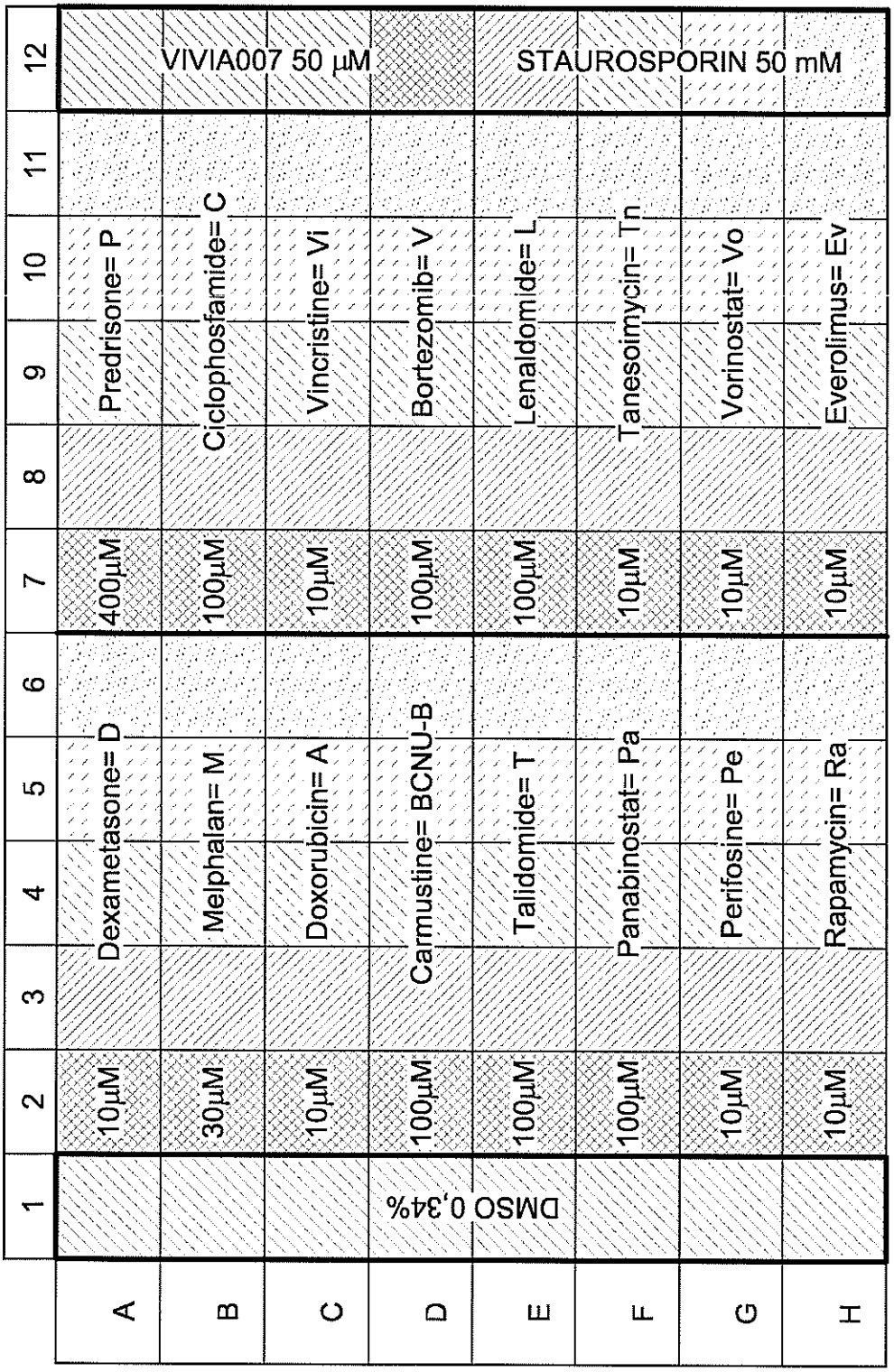

1 2 3 4 5 6 7 8 9 10 11 12
A
B
C
D
E
F
G
H
DMSO 0,34%
VIVIA007 50 µM
STAUROSPORIN 50 mM
10µM
30µM
10µM
100µM
100µM
100µM
10µM
10µM
Dexametasone= D
Melphalan= M
Doxorubicin= A
Carmustine= BCNU-B
Talidomide= T
Panabinostat= Pa
Perifosine= Pe
Rapamycin= Ra
400µM
100µM
10µM
100µM
100µM
10µM
10µM
10µM
Predrisone= P
Ciclophosfamide= C
Vincristine= Vi
Bortezomib= V
Lenaldomide= L
Tanesoimycin= Tn
Vorinostat= Vo
Everolimus= Ev

FIG. 14A

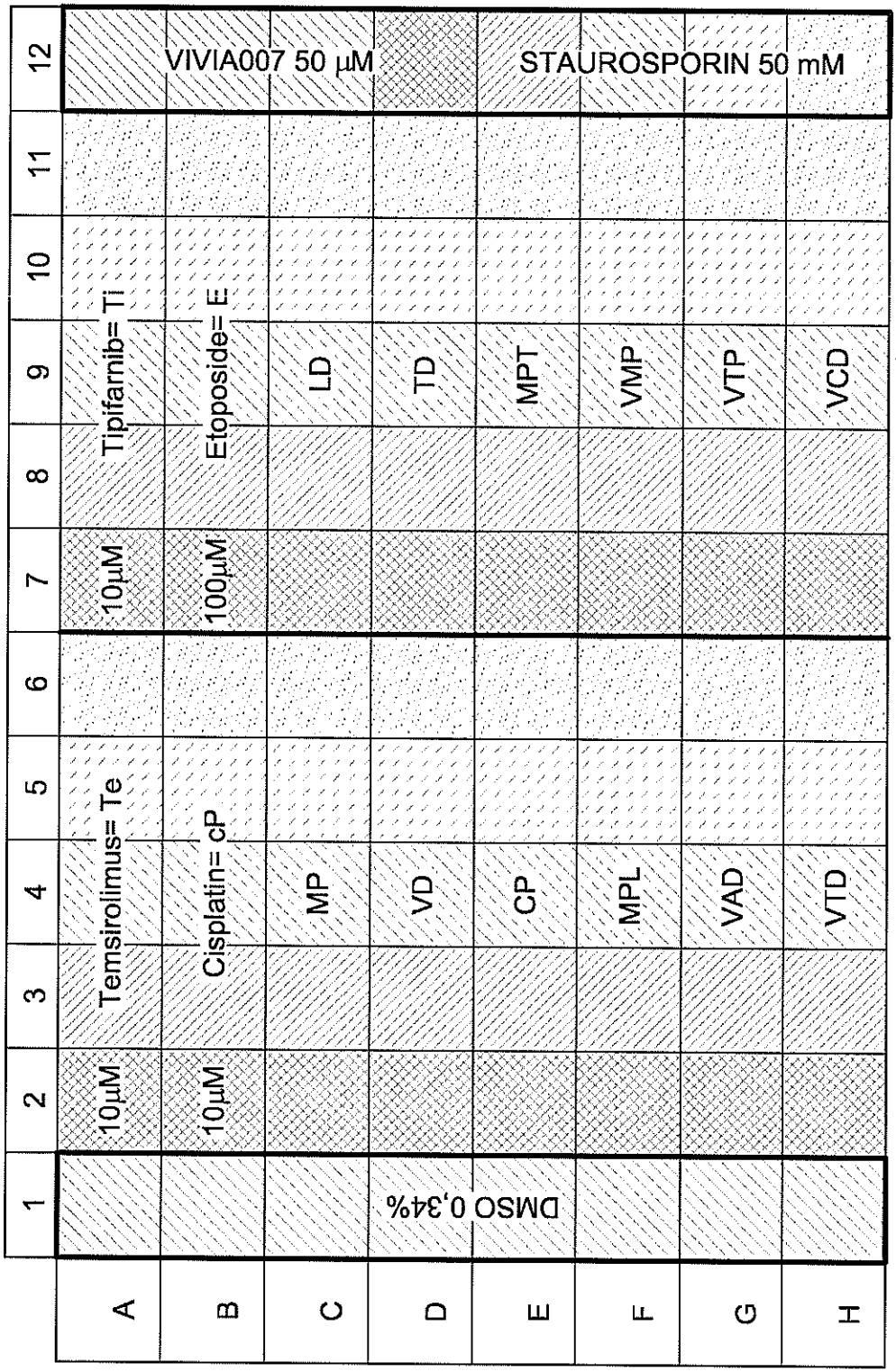

1
2
3
4
5
6
7
8
9
10
11
12
A
B
C
D
E
F
G
H
DMSO 0,34%
10µM
Temsirolimus= Te
Cisplatin= cP
10µM
100µM
Tipifarnib= Ti
Etoposide= E
MP
VD
CP
MPL
VAD
VTD
LD
TD
MPT
VMP
VTP
VCD
VIVIA007 50 µM
STAUROSPORIN 50 mM

FIG. 14B

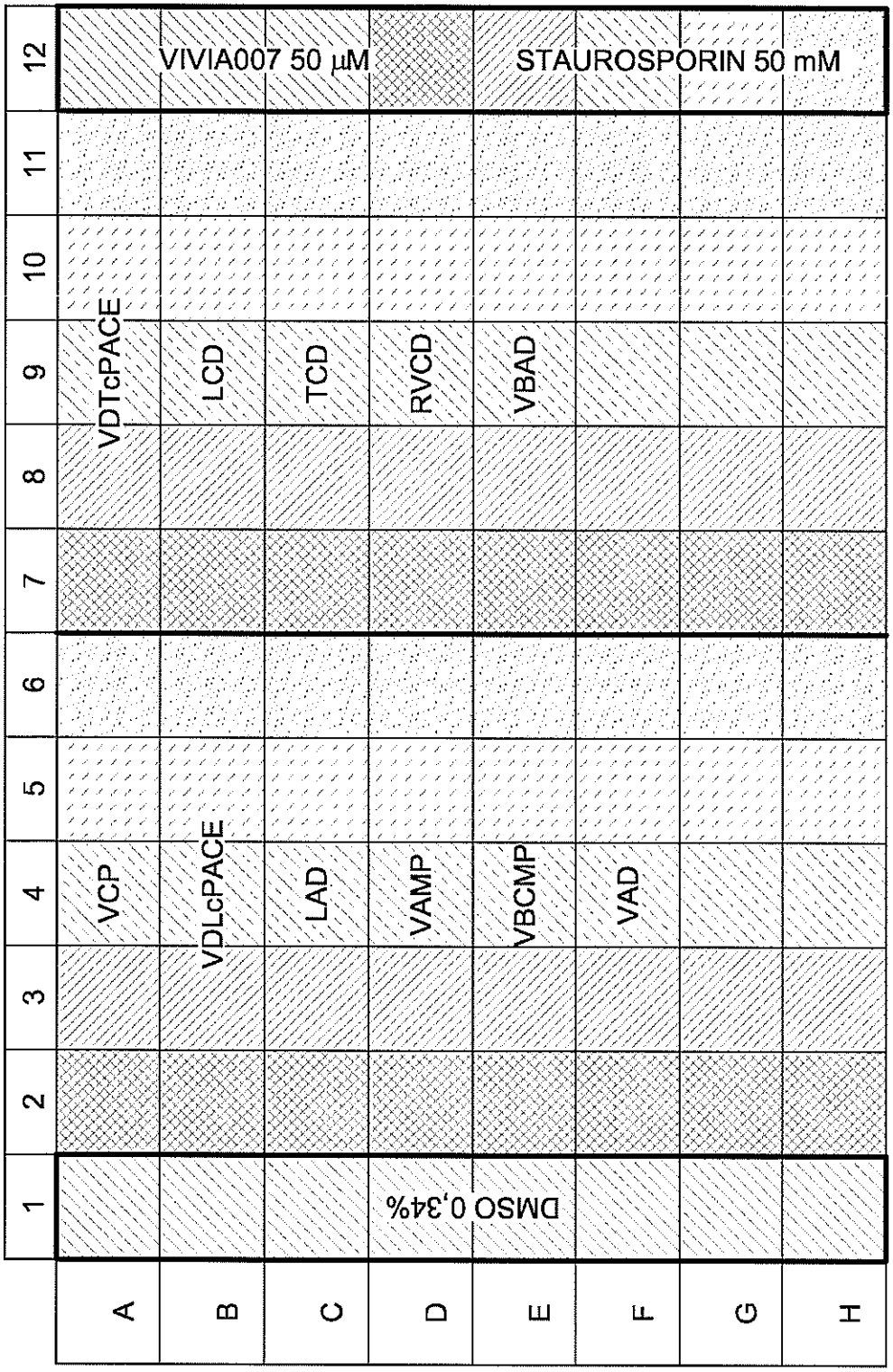

VIVIA007 50 µM
STAUROSPORIN 50 mM
VDTcPACE
LCD
TCD
RVCD
VBAD
VCP
VDLcPACE
LAD
VAMP
VBCMP
VAD
DMSO 0.34%
1
2
3
4
5
6
7
8
9
10
11
12
A
B
C
D
E
F
G
H

FIG. 14C

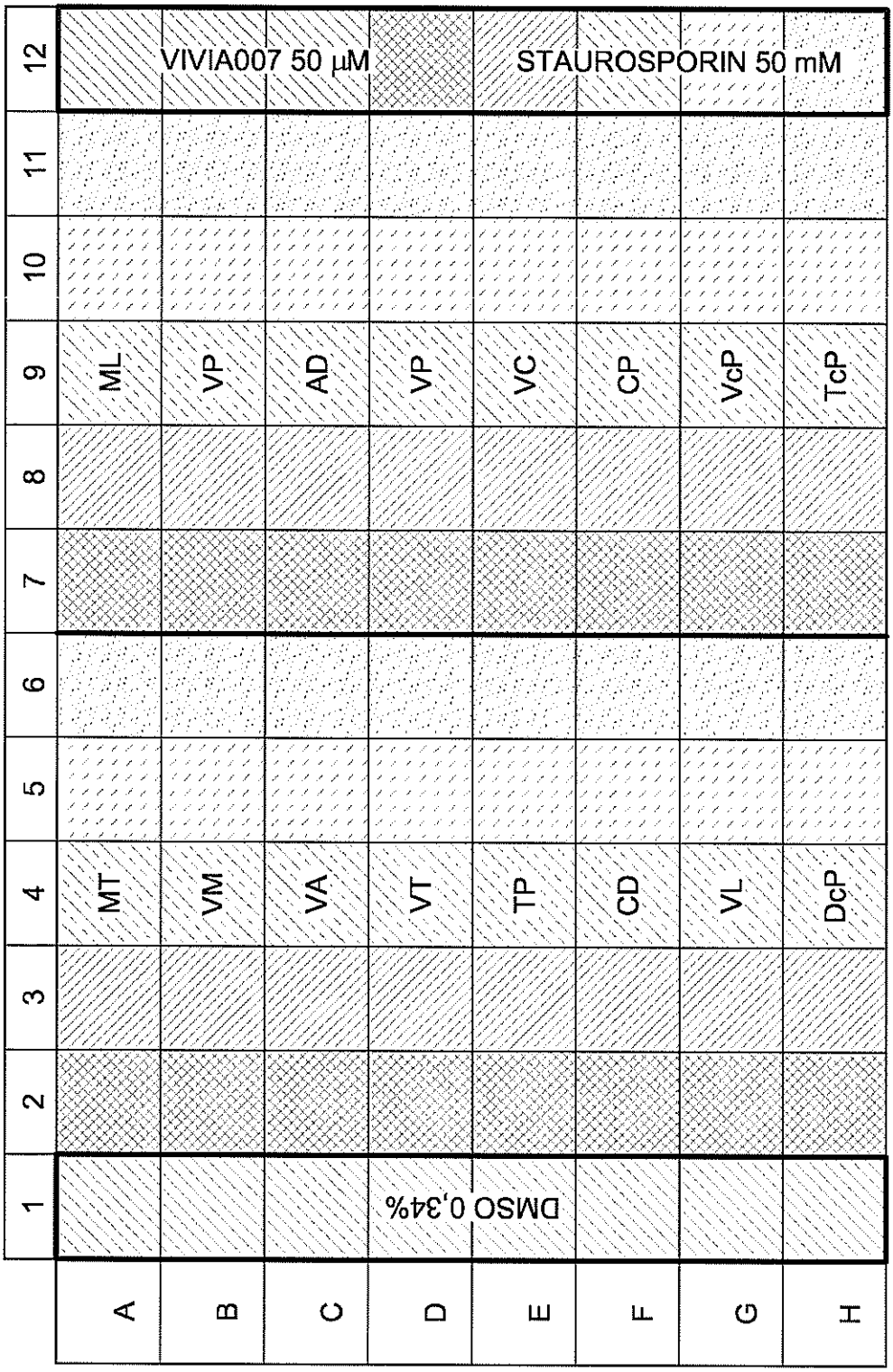

12
11
10
9
8
7
6
5
4
3
2
1
VIVIA007 50 µM
STAUROSPORIN 50 mM
ML
VP
AD
VP
VC
CP
VcP
TcP
MT
VM
VA
VT
TP
CD
VL
DcP
DMSO 0,34%
A
B
C
D
E
F
G
H

FIG. 14D

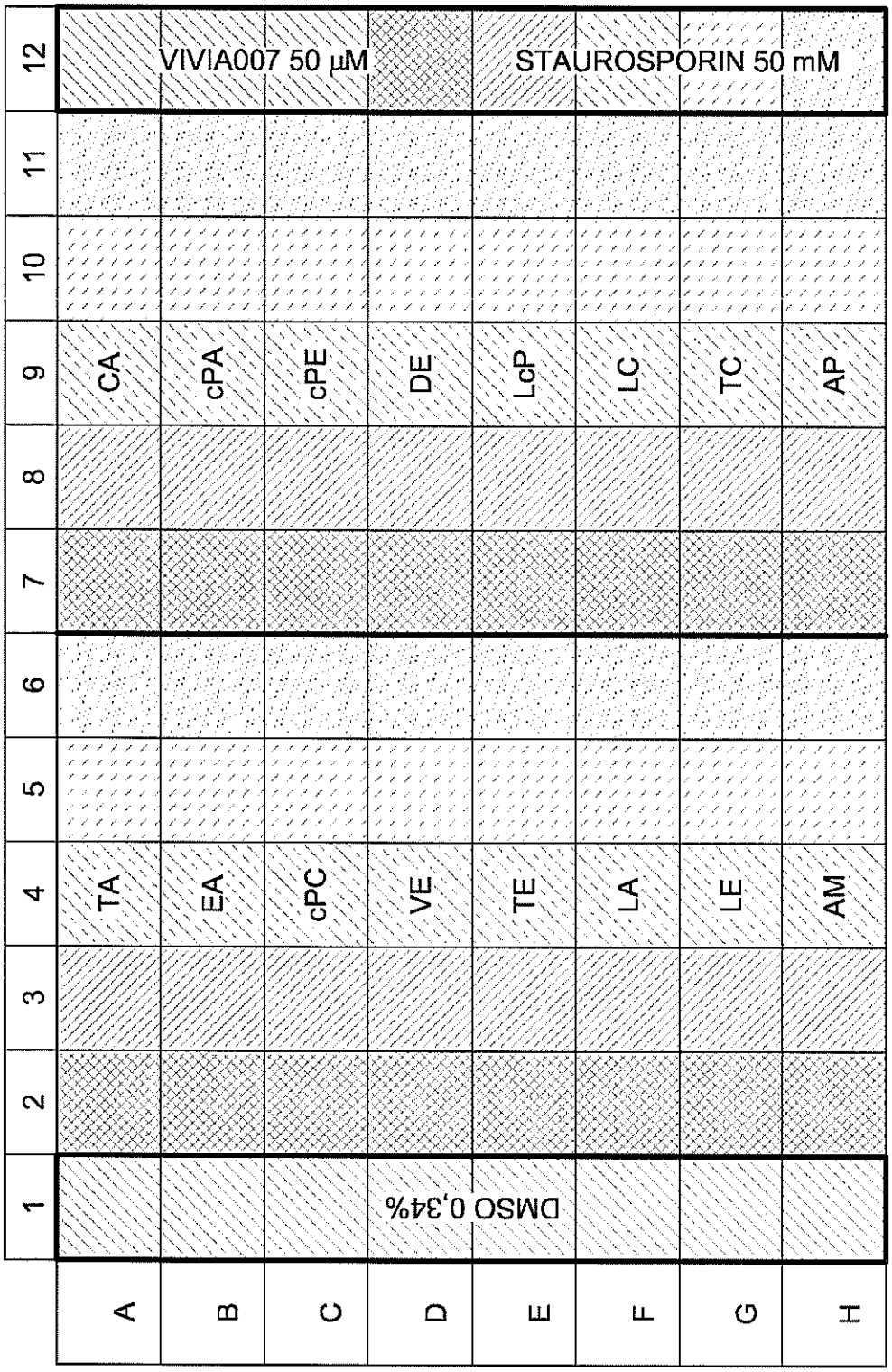

VIVIA007 50 µM
STAUROSPORIN 50 mM
DMSO 0,34%
CA
cPA
cPE
DE
LcP
LC
TC
AP
TA
EA
cPC
VE
TE
LA
LE
AM
1
2
3
4
5
6
7
8
9
10
11
12
A
B
C
D
E
F
G
H

FIG. 14E

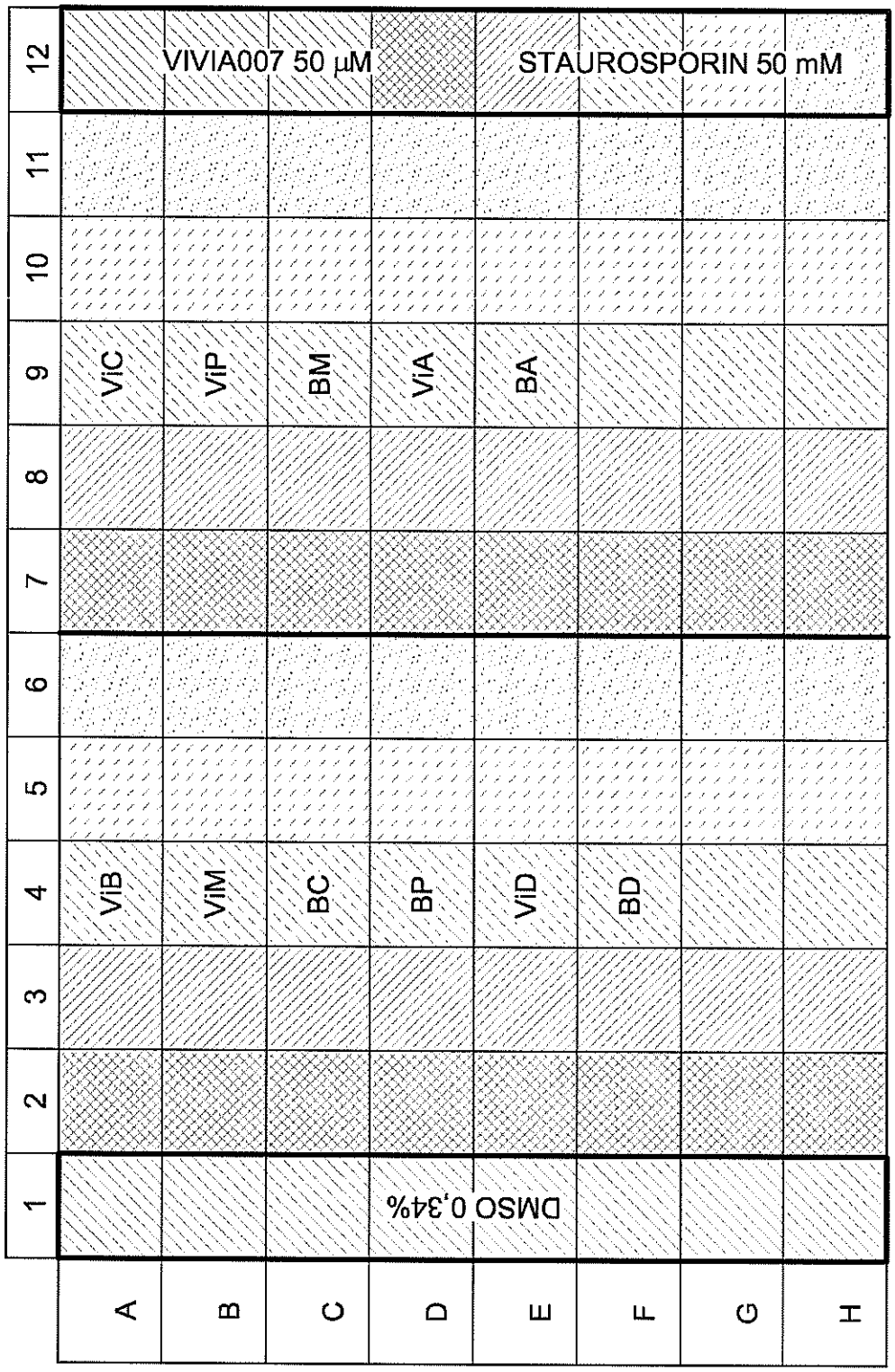
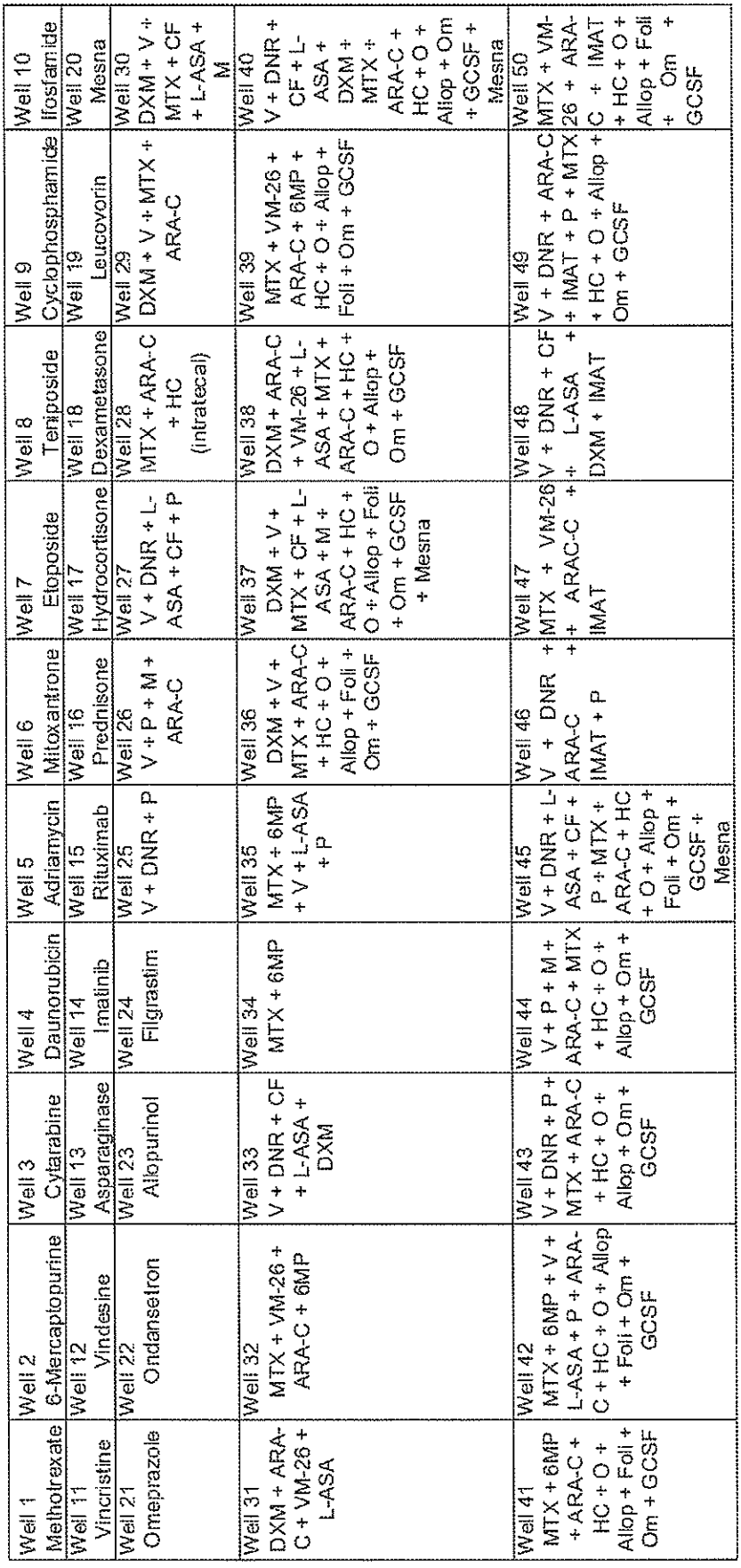

12
11
10
9
8
7
6
5
4
3
2
1
VIVIA007 50 µM
STAUROSPORIN 50 mM
ViC
ViP
BM
ViA
BA
ViB
ViM
BC
BP
ViD
BD
DMSO 0,34%
A
B
C
D
E
F
G
H

FIG. 14F



Well 1 Methotrexate	Well 2 6-Mercaptopurine	Well 3 Cytarabine	Well 4 Daunorubicin	Well 5 Adriamycin	Well 6 Mitoxantrone	Well 7 Etoposide	Well 8 Teniposide	Well 9 Cyclophosphamide	Well 10 Ifosfamide
Well 11 Vincristine	Well 12 Vindesine	Well 13 Asparaginase	Well 14 Imatinib	Well 15 Rituximab	Well 16 Prednisone	Well 17 Hydrocortisone	Well 18 Dexametasone	Well 19 Leucovorin	Well 20 Mesna
Well 21 Omeprazole	Well 22 Ondansetron	Well 23 Allopurinol	Well 24 Filgrastim	Well 25 V + DNR + P	Well 26 V + P + M + ARA-C	Well 27 V + DNR + L-ASA + CF + P	Well 28 MTX + ARA-C + HC (intratecal)	Well 29 DXM + V + MTX + ARA-C	Well 30 DXM + V + MTX + CF + L-ASA + M
Well 31 DXM + ARA-C + VM-26 + L-ASA	Well 32 MTX + VM-26 + ARA-C + 6MP	Well 33 V + DNR + CF + L-ASA + DXM	Well 34 MTX + 6MP	Well 35 MTX + 6MP + V + L-ASA + P	Well 36 DXM + V + MTX + ARA-C + HC + O + Allop + Foli + Om + GCSF	Well 37 DXM + V + MTX + CF + L-ASA + M + ARA-C + HC + O + Allop + Foli + Om + GCSF + Mesna	Well 38 DXM + ARA-C + VM-26 + L-ASA + MTX + ARA-C + HC + O + Allop + Om + GCSF	Well 39 MTX + VM-26 + ARA-C + 6MP + HC + O + Allop + Foli + Om + GCSF	Well 40 V + DNR + CF + L-ASA + DXM + MTX + ARA-C + HC + O + Allop + Om + GCSF + Mesna
Well 41 MTX + 6MP + ARA-C + HC + O + Allop + Foli + Om + GCSF	Well 42 MTX + 6MP + V + L-ASA + P + ARA-C + HC + O + Allop + Foli + Om + GCSF	Well 43 V + DNR + P + MTX + ARA-C + HC + O + Allop + Om + GCSF	Well 44 V + P + M + ARA-C + MTX + HC + O + Allop + Om + GCSF	Well 45 V + DNR + L-ASA + CF + P + MTX + ARA-C + HC + O + Allop + Foli + Om + GCSF + Mesna	Well 46 V + DNR + ARA-C + IMAT + P	Well 47 MTX + VM-26 + ARAC-C + IMAT	Well 48 V + DNR + CF + L-ASA + DXM + IMAT	Well 49 V + DNR + ARA-C + IMAT + P + MTX + HC + O + Allop + Om + GCSF	Well 50 MTX + VM-26 + ARA-C + IMAT + HC + O + Allop + Foli + Om + GCSF

FIG. 15

Well 51	Well 52	Well 53	Well 54	Well 55	Well 56	Well 57	Well 58	Well 59	Well 60
V + DNR + CF + L-ASA + DXM + IMAT + MTX + ARA-C + HC + O + Allop + Om + GCSF + Mesna	CF + P	R + DXM + V + IFOS + MTX + VM-26 + ARA-C	R + DXM + V + CF + MTX + ADRIA	R + DXM + VIND + MTX + VP-16 + ARA-C	R + DXM + MTX + IFOS + ARA-C + VM-26	R + DXM + MTX + CF + ADRIA	CF + P + MTX + ARA-C + HC + O + Allop + Om + GCSF + Mesna	R + DXM + V + IFOS + MTX + VM-26 + ARA-C + HC + O + Foli + Allop + Om + GCSF + Mesna	R + DXM + V + MTX + CF + ADRIA + ARA-C + HC + O + Foli + Allop + Om + GCSF + Mesna
Well 61	Well 62	Well 63	Well 64	Well 65	Well 66	Well 67	Well 68	Well 69	Well 70
R + DXM + VIND + MTX + VP-16 + ARA-C + HC + O + Foli + Allop + Om + GCSF	R + DXM + MTX + IFOS + ARA-C + HC + O + Foli + Allop + Om + GCSF + Mesna	R + DXM + MTX + CF + ADRIA + ARA-C + HC + O + Foli + Allop + Om + GCSF + Mesna	V + M + MTX + DXM	V + MTX + ARA-C + DXM	V + MTX + L-ASA + DXM	M + MTX + ARA-C + DXM	M + MTX + L-ASA + DXM	6MP + ARA-C + MTX	6-MP + L-ASA + MTX
Well 71	Well 72	Well 73	Well 74	Well 75	Well 76	Well 77	Well 78	Well 79	Well 80
IMAT + V + DNR	IMAT + V + ARA-C	IMAT + L-ASA + V	IMAT + CF + V	R + CF + P	R + V + IFOS	R + V + MTX	R + V + MTX + ARA-C + VM-26	R + VIND + VP-16	R + MTX + IFOS + VP-16 + ARA-C
Well 81	Well 82	Well 83	Well 84	Well 85	Well 86	Well 87	Well 88	Well 89	Well 90
V + M + MTX + DXM + ARA-C + O + Foli + Om + GCSF	V + MTX + ARA-C + O + Allop + GCSF	V + MTX + L-ASA + DXM + ARA-C + O + Foli + Allop + Om + GCSF	M + MTX + ARA-C + DXM + O + Allop + Foli + Om + GCSF	M + MTX + L-ASA + DXM + ARA-C + O + Allop + Foli + Om + GCSF	6MP + ARA-C + MTX + HC + O + Allop + Om + GCSF	6MP + L-ASA + ARA-C + HC + O + Allop + Foli + Om + GCSF	IMAT + V + DNR + MTX + ARA-C + HC + O + Allop + Foli + Om + GCSF	R + V + MTX + ARA-C + HC + O + Allop + Foli + Om + GCSF	R + V + MTX + ARA-C + HC + O + Allop + Foli + Om + GCSF

FIG. 15 Continued

Well 91	Well 92	Well 93	Well 94	Well 95	Well 96	
R + VIND + VP-16 + MTX + ARA-C + HC + O + Allop + Foli + Om + GCSF	R + MTX + IFOS + VP-16 + ARA-C + HC + O + Allop + Foli + Om + GCSF + Mesna	IMAT + V + ARA-C + MTX + HC + O + Allop + Foli + Om + GCSF	IMAT + V + ARA-C + MTX + HC + O + Allop + Foli + Om + GCSF	IMAT + CF + V + MTX + ARA-C + HC + O + Allop + Foli + Om + GCSF + Mesna	R + CF + P + MTX + ARA-C + HC + O + Allop + Foli + Om + GCSF + Mesna	

FIG. 15 Continued

1° Apply drugs individually:

Well 1 Erythropoietin	Well 2 Filgrastim	Well 3 Talidomide
Well 4 Ciclosporin	Well 5 Tymoglogulin	Well 6 Arsenic Trioxide
Well 7 Azacitidine	Well 8 Decitabine	Well 9 Fludarabine
Well 10 Etoposide	Well 11 Citarabine	Well 12 Idarrubicine
Well 13 Carboplatin	Well 14 Prednisona	Well 15 Ondansetron
Well 16 Omeprazole	Well 17 Alopurinol	Well 18 Cotrimoxazol + Folic Acid

Cetlam SMD < 65 Years

Well 37 Ida + ARA-C + VP-16	Well 38 Ida + VP-16
Well 39 ARA-C + VP-16	Well 40 Ida + ARA-C + VP-16 + Ondan + Om + Alop
Well 41 Ida + VP-16 + Ondan + Om + Alop	Well 42 ARA-C + VP-16 + Ondan + Om + Alop

VP - 16: Etoposide

3° Combinations of other drugs used in

Well 52 Azacitidine + Ondans + Om + Alop	Well 53 Decitabine + Ondans + Om + Alop
Well 54 EPO + Filgrastim	Well 55 Talidomide + Ondans + Om + Alop
Well 56 Arsenic Trioxide + Ondan + Om + Alop	

EPO: Erythropoietin

2° Combine drugs following different Pethema SMD/98

Well 19 Fluda + ARA-C + Ida + GCSF	Well 20 Fluda + ARA-C
Well 21 Fluda + Ida	Well 22 Fluda + GCSF
Well 23 ARA-C + Ida	Well 24 ARA-C + GCSF
Well 25 Ida + GCSF	Well 26 ARA-C + Ida + GCSF
Well 27 Fluda + ARA-C + Ida + GCSF + Ondan + Om + Alop + Cotri + AcF	Well 28 Fluda + ARA-C + Ondan + Om + Alop + Cotri + AcF
Well 29 Fluda + Ida + Ondan + Om + Alop + Cotri + AcF	Well 30 Fluda + GCSF + Ondan + Om + Alop + Cotri + AcF
Well 31 ARA-C + Ida + Ondan + Om + Alop + Cotri + AcF	Well 32 ARA-C + GCSF + Ondan + Om + Alop + Cotri + AcF
Well 33 Ida + GCSF + Ondan + Om + Alop + Cotri + AcF	Well 34 ARA-C + Ida + GCSF + Ondan + Om + Alop + Cotri + AcF
Well 35 Carbop + GCSF	Well 36 Carbop + GCSF + Ondan + Om + Alop + Cotri + AcF

Fluda: Fludarabine ARA-C: Citarabine
Ida: Idarrubicine GCSF: Filgrastim
Carbop: Carboplatin

Pethema ATG-CsA 2002

Well 43 ATG + CsA + Pred	Well 44 ATG + CsA
Well 46 CsA + Pred	Well 47 ATG + Paracet + Polar
Well 48 ATG + CsA + Pred + Ondan + Om + Alop	Well 50 ATG + Pred + Ondan + Om + Alop
Well 51 CsA + Pred + Ondan + Om + Alop	

ATG: Antimimocitic rabbit globulin of thymoglobulin
CsA: Cyclosporin Pred: Prednisone

FIG. 16

Well 1 Daunorubicin	Well 2 Idarubicin	Well 3 ARA-C	Well 4 Mitoxantrone	Well 5 Etoposide	Well 6 Fludarabbine	Well 7 Dauno + ARA-C	Well 8 Ida + ARA-C	Well 9 Fluda + Ida + ARA-C + GCSF	Well 10 Fluda + Ida
Well 11 Fluda + ARA-C	Well 12 Fluda + GCSF	Well 13 Fluda + Ida + GCSF	Well 14 Fluda + ARA-C + GCSF	Well 15 Ida + ARA-C + VP16	Well 16 Ida + VP16	Well 17 VP16 + ARA-C	Well 18 Mitox + ARA-C	Well 19 Dauno + Om + Ondans + Alop	Well 20 Ida + Om + Ondans + Alop
Well 21 ARA-C + Om + Ondans	Well 22 Mitox + Om + Ondans + Alop	Well 23 VP16 + Om + Ondans + Alop	Well 24 Fluda + Om + Ondans + Alop + Cotri + AcF	Well 25 Dauno + ARA-C + Om + Ondans + Alop	Well 26 Ida + ARA-C + Om + Ondans + Alop	Well 27 Fluda + Ida + ARA-C + GCSF + Om + Ondans + Alop + Cotri + AcF	Well 28 Fluda + Ida + Om + Ondans + Alop + Cotri + AcF	Well 29 Fluda + ARA-C + Om + Ondans + Alop + Cotri + AcF	Well 30 Fluda + GCSF + Om + Ondans + Alop + Cotri + AcF
Well 31 Fluda + Ida + GCSF + Om + Ondans + Alop + Cotri + AcF	Well 32 Fluda + ARA-C + GCSF + Om + Ondans + Alop + Cotri + AcF	Well 33 Ida + ARA-C + VP16 + Om + Ondans + Alop	Well 34 Ida + VP16 + Om + Ondans + Alop	Well 35 VP16 + ARA-C + Om + Ondans + Alop	Well 36 Mitox + ARA-C + Om + Ondans + Alop	Well 37 Amascrine *	Well 38 Carboplatin	Well 39 AMSA + ARA-C	Well 40 ARA-C + Ida + GCSF
Well 41 Ida + GCSF	Well 42 Carbop + GCSF	Well 43 AMSA + Om + Ondans + Alop	Well 44 Carbop + Om + Ondans + Alop	Well 45 AMSA + ARA-C + Om + Ondans + Alop	Well 46 ARA-C + Ida + GCSF + Om + Ondans + Alop + Cotri + AcF	Well 47 Ida + GCSF + Om + Ondans + Alop	Well 48 Carbop + GCSF + Om + Ondans + Alop + Cotri + AcF	Well 49 Dauno lipo	Well 50 Dauno lipo + ARA-C
Well 51 Mitox + ARA-C + VP-16	Well 52 Mitox + VP-16	Well 53 Dauno lipo + Mitox	Well 54 Dauno lipo + VP-16	Well 55 Dauno lipo + Om + Ondans + Alop	Well 56 Dauno lipo + ARA-C + Om + Ondans + Alop	Well 57 Mitox + ARA-C + VP-16 + Om + Ondans + Alop	Well 58 Mitox + VP-16 + Om + Ondans + Alop	Well 59 Dauno lipo + Mitox + Om + Ondans + Alop	Well 60 Dauno lipo + VP-16 + Om + Ondans + Alop
Well 61 Dauno + Fluda	Well 62 Dauno + Carop	Well 63 Dauno lipo + Fluda	Well 64 Dauno lipo + Carop	Well 65 Fluda + Carbop	Well 66 Dauno + Mitox	Well 67 Dauno + VP-16	Well 68 Dauno + AMSA	Well 69 Ida + Mitox	Well 70 Ida + AMSA

FIG. 17

Well 71 Ida + Carbop	Well 72 Fluda + Mitox	Well 73 Fluda + VP-16	Well 74 Mitox + AMSA	Well 75 Mitox + Carbop	Well 76 VP-16 + AMSA	Well 77 VP-16 + Carbop	Well 78 AMSA + Fluda	Well 79 6-Mercaptopurina	Well 80 Hidroxiure a
Well 81 Ondansetron	Well 82 Alopurinol	Well 83 Omeprazole	Well 84 GCSF	Well 85 Catrimoxazol e	Well 86 Om + Ondans + Alop	Well 87 Om + Ondans + Alop + Ctori + AcF	Well 88 GO	Well 89 GO + ARA-C	Well 90 GO + Ida + ARA-C
Well 91 GO	Well 92 GO + Om + Ondans + Alop	Well 93 GO + ARA-C + Om + Ondans + Alop	Well 94 GO + Ida + ARA-C + Om + Ondans + Alop	Well 95 GO + Ida + Om + Ondans + Alop					

FIG. 17 Continued

Well 1 Tretinoin	Well 2 Idarubicin	Well 3 Mitoxantrone	Well 4 Citarabine	Well 5 6-Mercaptopurine	Well 6 Methotrexate	Well 7 Ondansetron	Well 8 Allopurinol	Well 9 Omeprazole	Well 10 Dexamethasone
Well 11 ATRA + Ida	Well 12 ATRA + Ida + Ondans + Alop + Om	Well 13 ATRA + Ida + Ondans + Alop + Om +Dexa	Well 14 ATRA + Mitox	Well 15 ATRA + Ida + ARA-C	Well 16 ATRA + ARA-C	Well 17 Ida + ARA-C	Well 18 Ida + Mitox	Well 19 ATRA + Mitox + Ondans + Alop + Om	Well 20 ATRA + Ida + ARA-C + Ondans + Alop + Om
Well 21 ATRA +ARA-C + Ondans + Alop + Om	Well 22 Ida + ARA-C + Ondans + Alop + Om	Well 23 Ida + Mitox + Ondans + Alop + Om	Well 24 6-MP + MTX + ATRA	Well 25 6-MP + MTX	Well 26 ATRA + 6-MP	Well 27 ATRA + MTX	Well 28 6-MP + MTX + ATRA + Om	Well 29 6-MP + MTX + Om	Well 30 ATRA + 6-MP + Om
Well 31 ATRA + MTX + Om	Well 32 ARA-C + Mitox + ATRA	Well 33 ARA-C + Mitox	Well 34 ARA-C + Mitox + ATRA + Ondans + Alop + Om	Well 35 ARA-C + Mitox + Ondans + Alop + Om	Well 36 ATRA + Daunro +	Well 37 ATRA + VP-16	Well 38 ATRA + Fluda	Well 39 ATRA + Carbop	Well 40 Daunо lipo
Well 41 ATRA + Dauno + Ondans + Alop + Om	Well 42 ATRA + VP-16 + Ondans + Alop + Om	Well 43 ATRA + Fluda + Ondans + Alop + Om + Cotri + FAc	Well 44 ATRA + Carbop + Ondans + Alop + Om	Well 45 ATRA + Dauno lipo + Ondans + Alop + Om					

FIG. 18

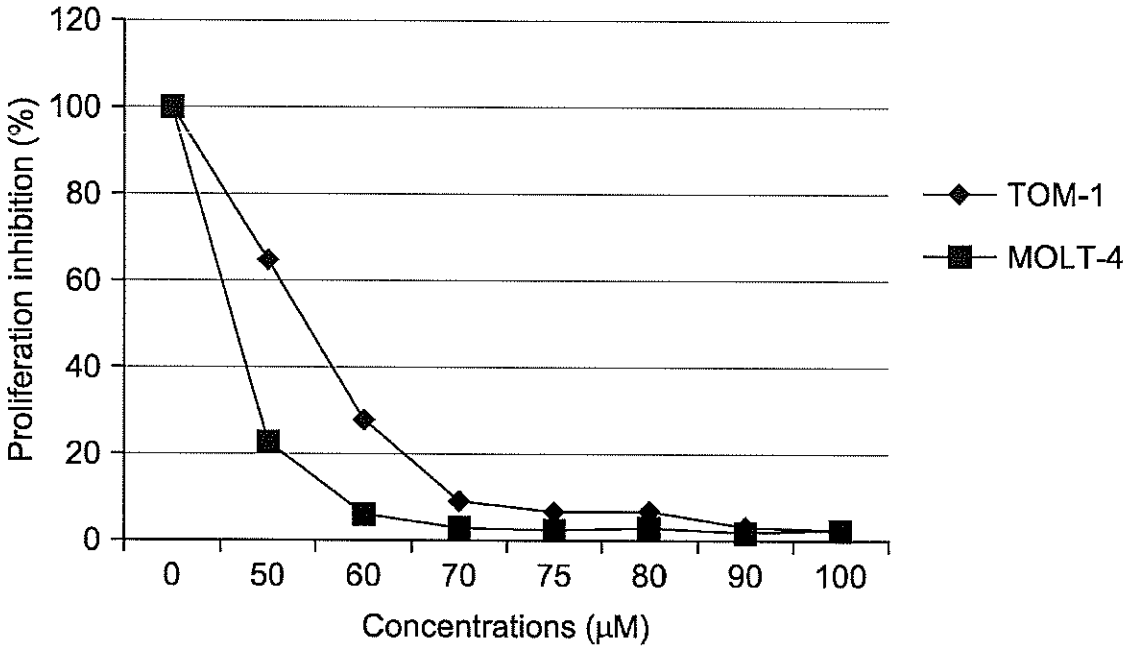

120
100
80
60
40
20
0
Proliferation inhibition (%)
0
50
60
70
75
80
90
100
Concentrations (μM)
TOM-1
MOLT-4

FIG. 19

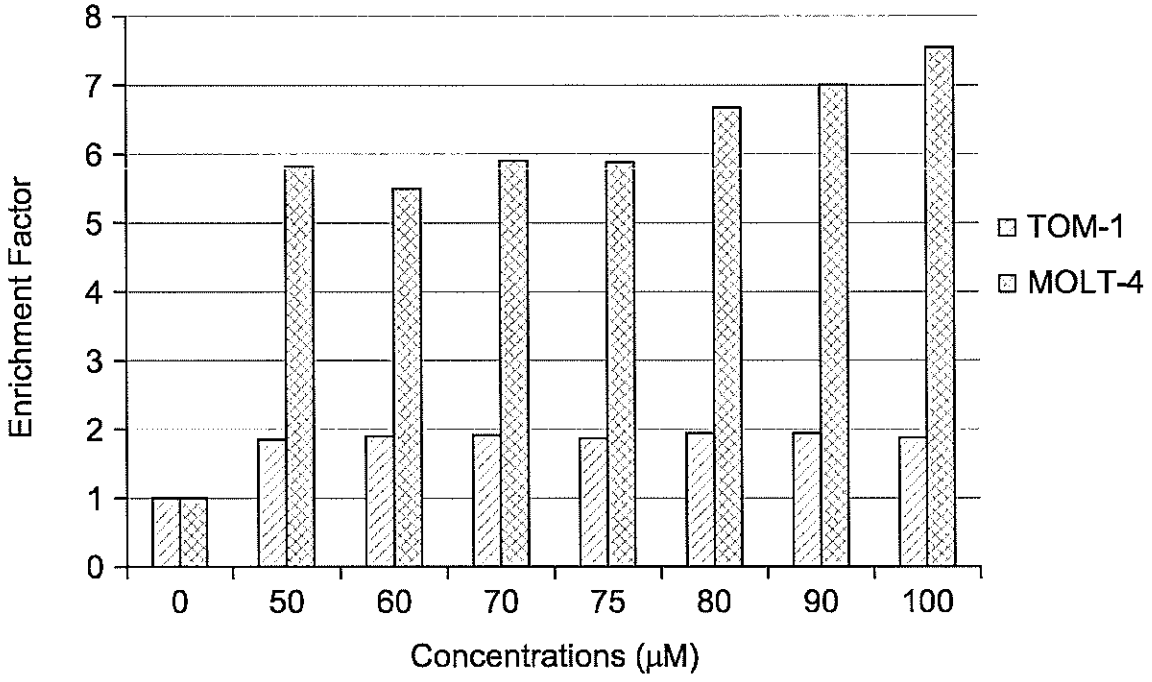

Enrichment Factor
8
7
6
5
4
3
2
1
0
0
50
60
70
75
80
90
100
Concentrations (μM)
TOM-1
MOLT-4

FIG. 20

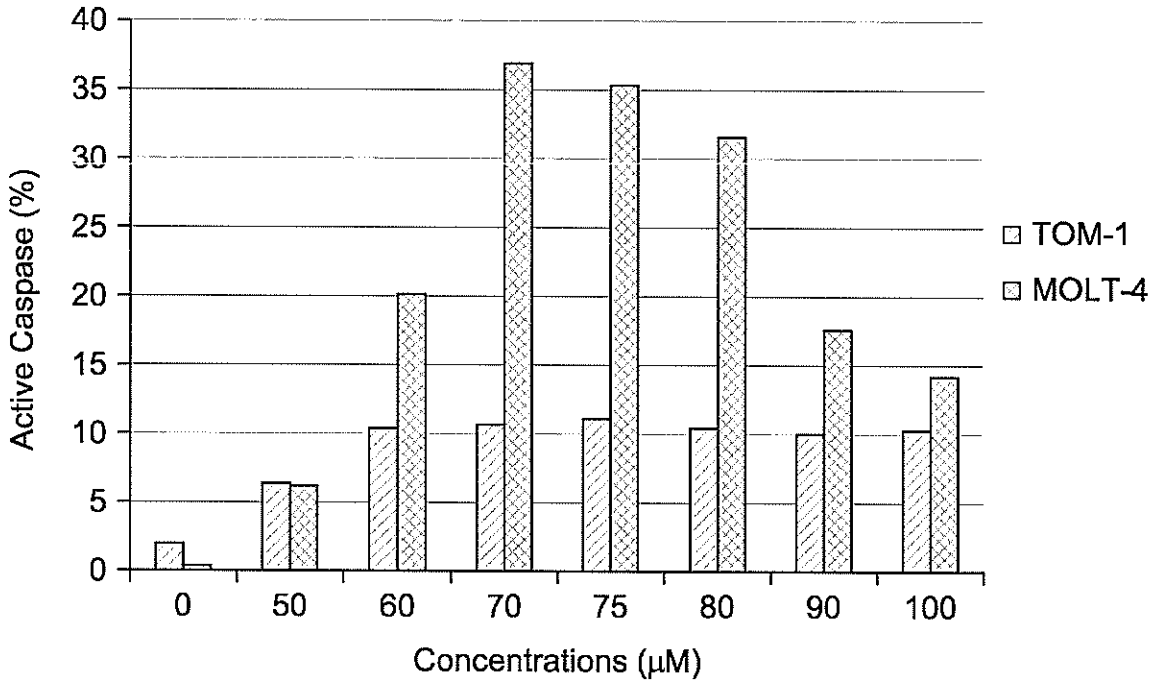

40
35
30
25
20
15
10
5
0
Active Caspase (%)
0
50
60
70
75
80
90
100
Concentrations (μM)
TOM-1
MOLT-4

FIG. 21

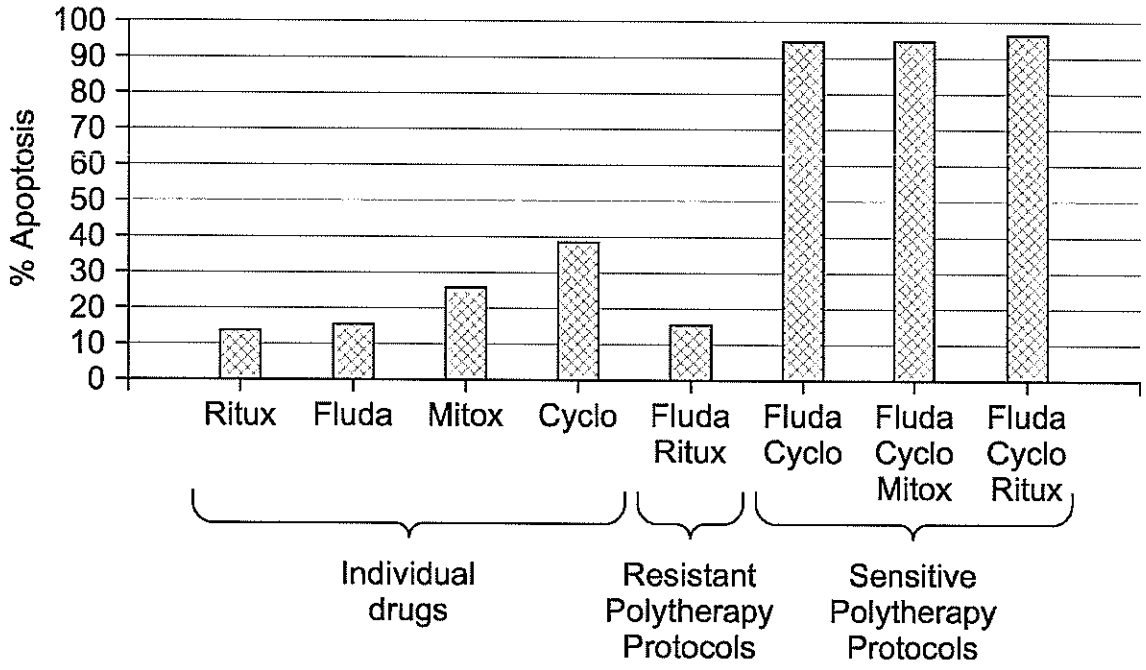

100
90
80
70
60
50
40
30
20
10
0
% Apoptosis
Ritux
Fluda
Mitox
Cyclo
Fluda Ritux
Fluda Cyclo
Fluda Cyclo Mitox
Fluda Cyclo Ritux
Individual drugs
Resistant Polytherapy Protocols
Sensitive Polytherapy Protocols

FIG. 22

(μM)	Fludarabine	Cyclophosphamide
1	1	30
2	0.33	10
3	0.11	3.33
4	0.037	1.11
5	0.012	0.37

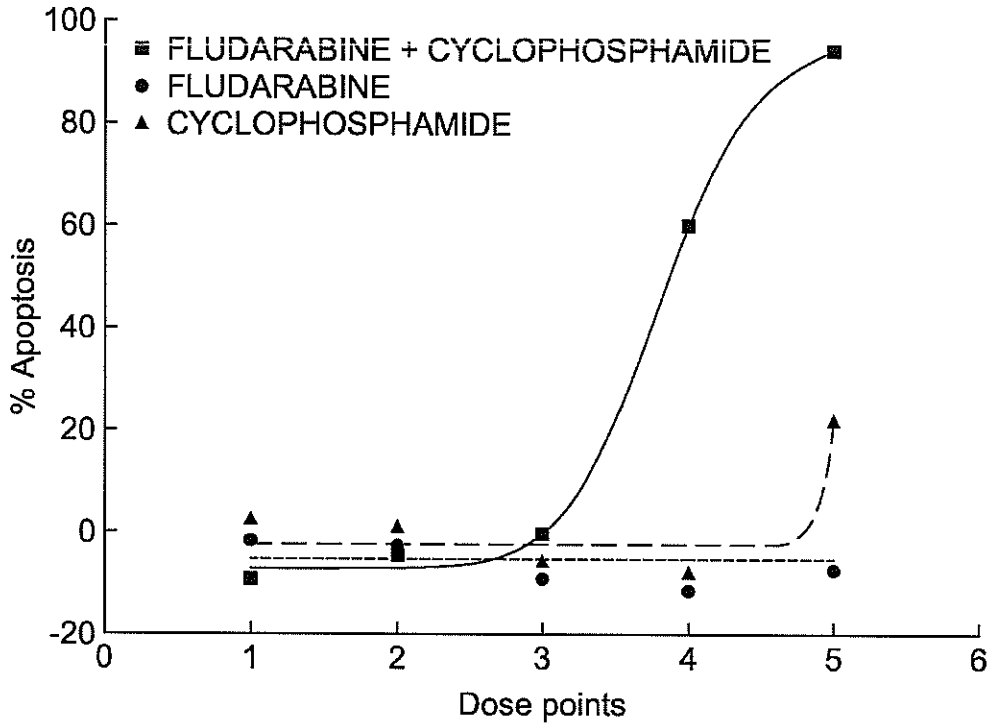


FIG. 23

(μM)	Fludarabine	Cyclophosphamide	Mitoxantrone
1	1	30	1
2	0.33	10	0.33
3	0.11	3.33	0.11
4	0.037	1.11	0.037

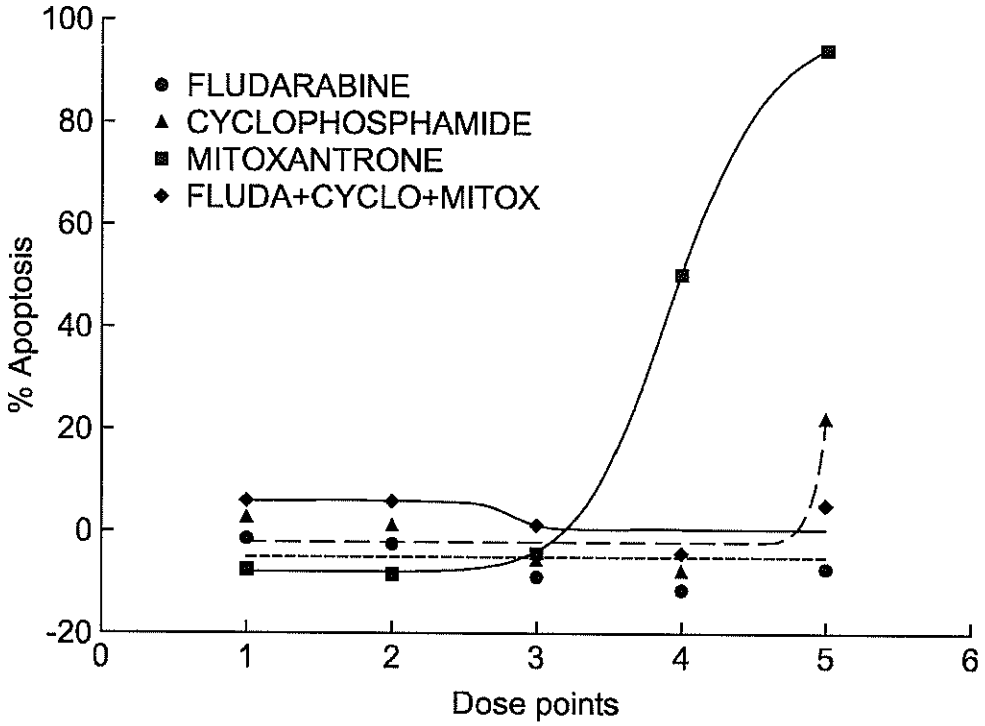


FIG. 24

(μM)	Fludarabine	Cyclophosphamide	Rituximab
1	1	30	30
2	0.33	10	10
3	0.11	3.33	3.33
4	0.037	1.11	1.11
5	0.012	0.37	0.37

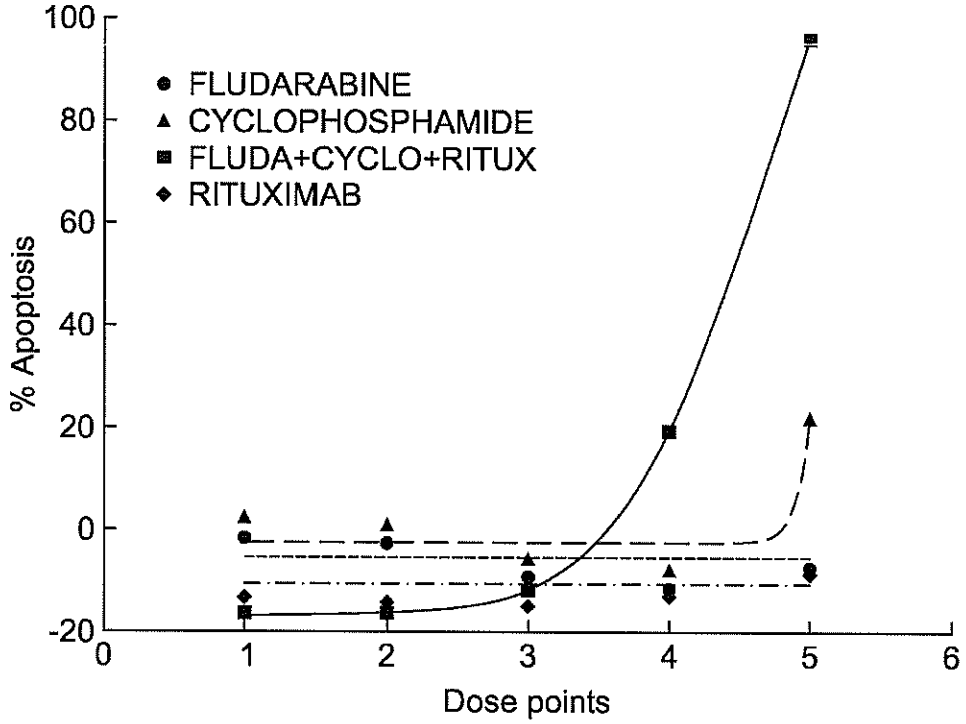


FIG. 25

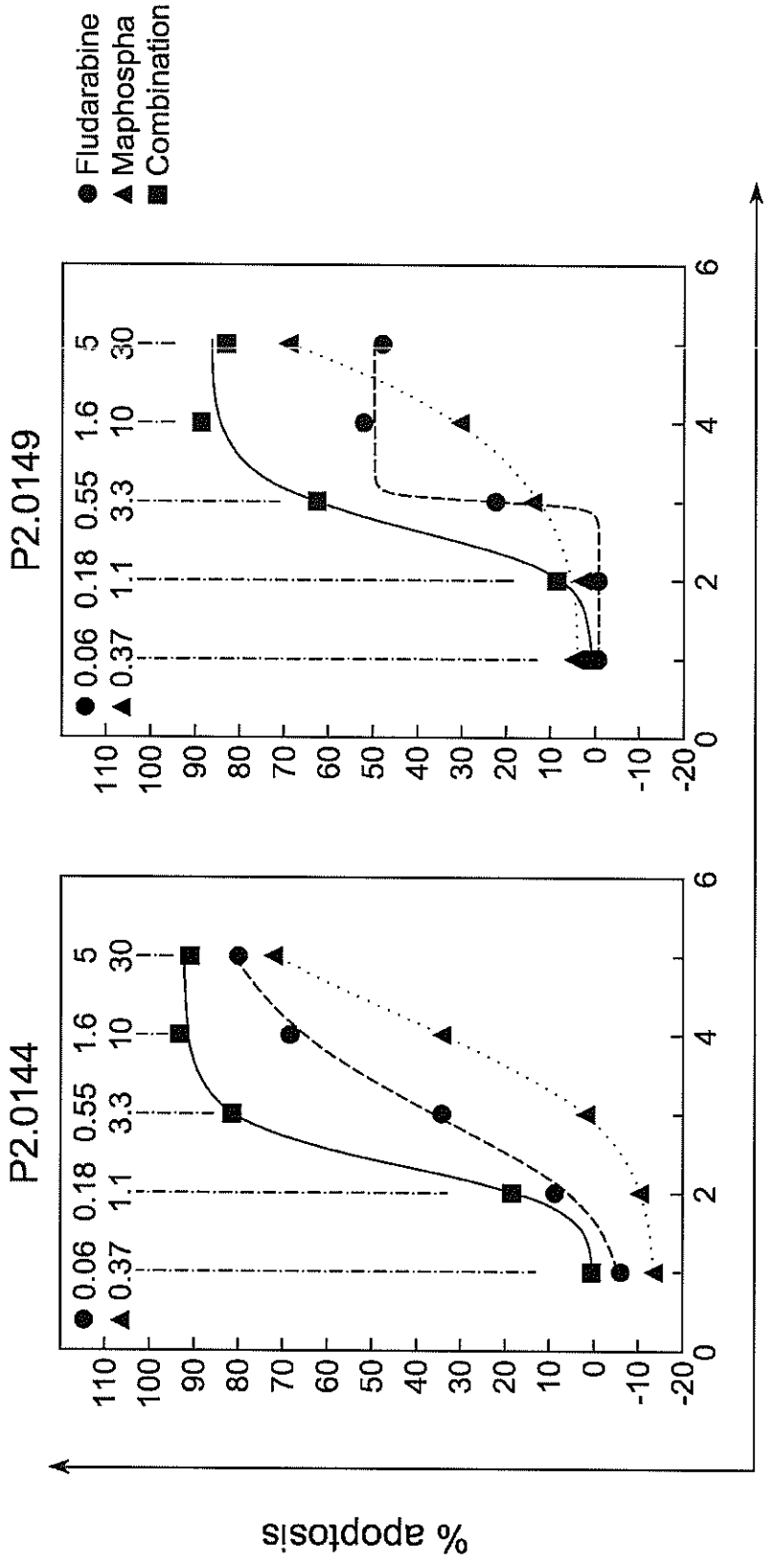
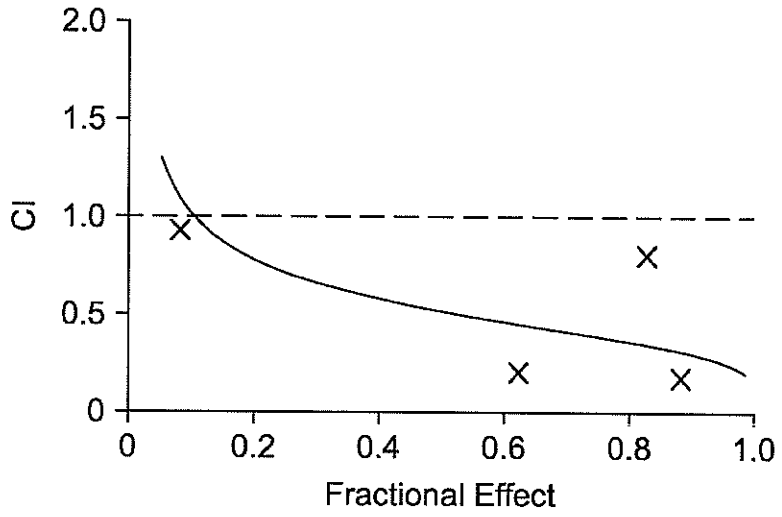
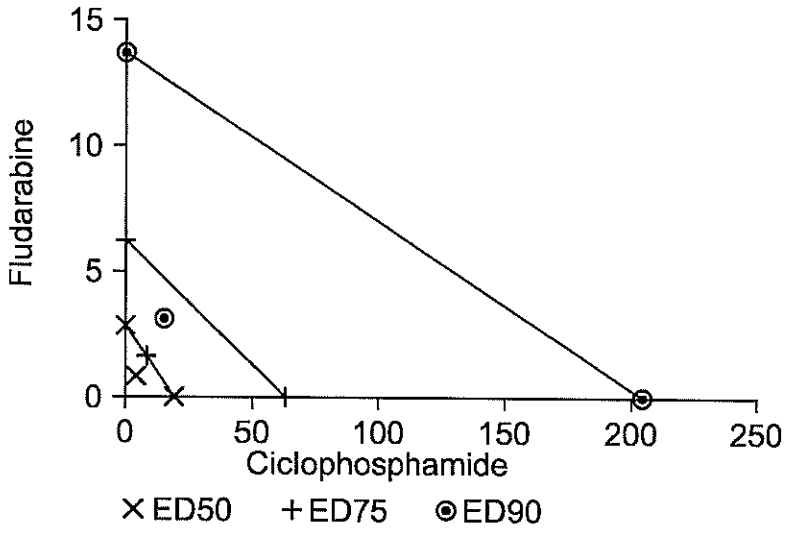

Fludarabine
Maphospha
Combination
P2.0149
P2.0144
0.06
0.37
0.18
1.1
0.55
3.3
1.6
10
5
30
% apoptosis
Doses (μM)

FIG. 26





Summary results					
Fraction affected	CI (+4)	Fludarabine dose (μM)	Ciclophosphamide dose (μM)	DRI (+2) Fludarabine	DRI (+2) Ciclophosphamide
0.50	0.961	2.86	19.54	3.324	4.541
0.75	0.393	6.25	63.19	3.802	7.681
0.90	0.166	13.67	204.23	4.348	12.99

FIG. 27

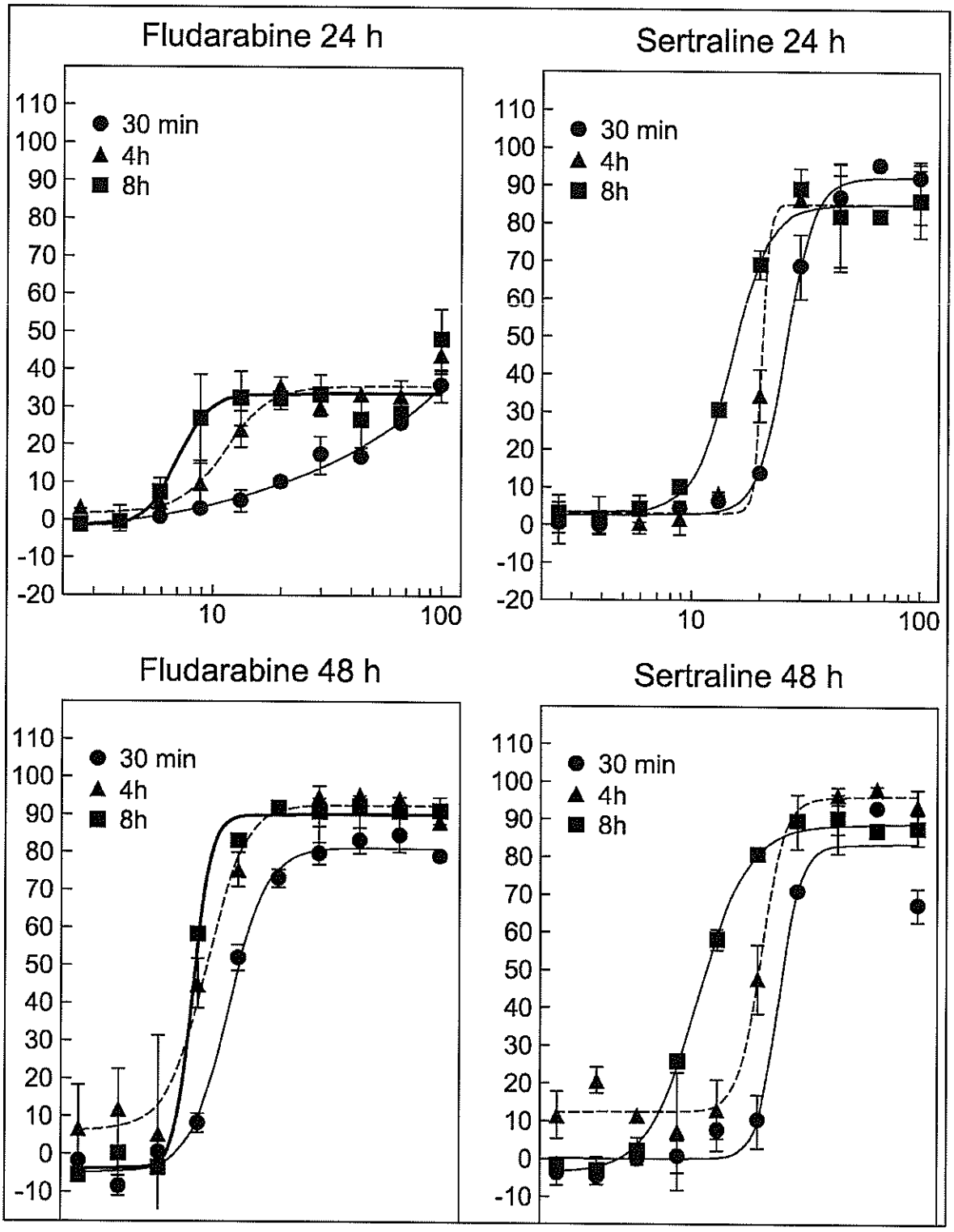

Fludarabine 24 h
Sertraline 24 h
Fludarabine 48 h
Sertraline 48 h
30 min
4h
8h
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
10
100

FIG. 28

	2	3	4	5	6	7	8	9	10	11	12	13	14	15
1	1,2	1,3	1,4	1,5	1,6	1,7	1,8	1,9	1,10	1,11	1,12	1,13	1,14	1,15
2		2,3	2,4	2,5	2,6	2,7	2,8	2,9	2,10	2,11	2,12	2,13	2,14	2,15
3			3,4	3,5	3,6	3,7	3,8	3,9	3,10	3,11	3,12	3,13	3,14	3,15
4				4,5	4,6	4,7	4,8	4,9	4,10	4,11	4,12	4,13	4,14	4,15
5					5,6	5,7	5,8	5,9	5,10	5,11	5,12	5,13	5,14	5,15
6						6,7	6,8	6,9	6,10	6,11	6,12	6,13	6,14	6,15
7							7,8	7,9	7,10	7,11	7,12	7,13	7,14	7,15
8								8,9	8,10	8,11	8,12	8,13	8,14	8,15
9									9,10	9,11	9,12	9,13	9,14	9,15
10										10,11	10,12	10,13	10,14	10,15
11											11,12	11,13	11,14	11,15
12												12,13	12,14	12,15
13													13,14	13,15
14														14,15

FIG. 29

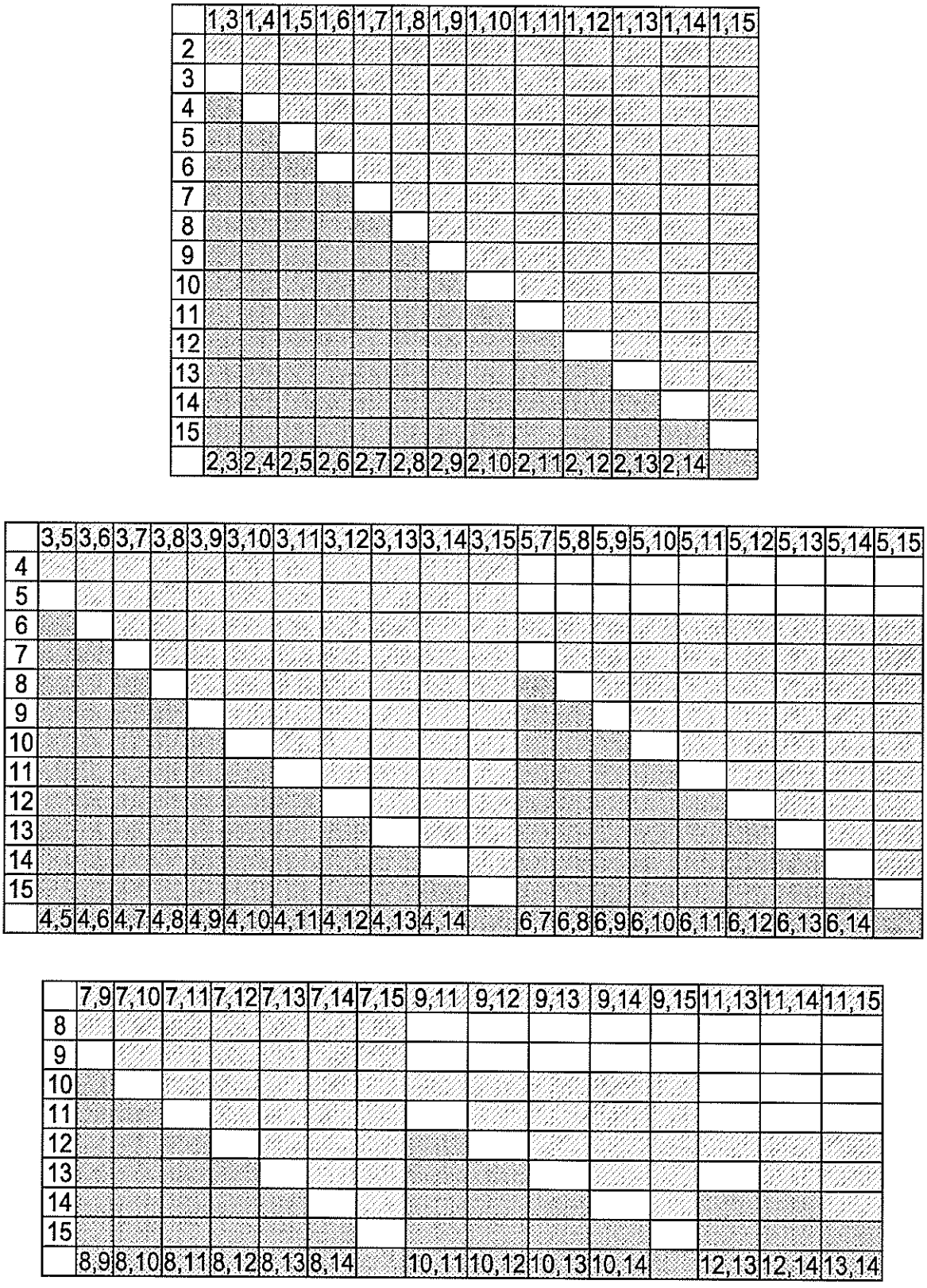

1,3 1,4 1,5 1,6 1,7 1,8 1,9 1,10 1,11 1,12 1,13 1,14 1,15
2 3 4 5 6 7 8 9 10 11 12 13 14 15
2,3 2,4 2,5 2,6 2,7 2,8 2,9 2,10 2,11 2,12 2,13 2,14
3,5 3,6 3,7 3,8 3,9 3,10 3,11 3,12 3,13 3,14 3,15 5,7 5,8 5,9 5,10 5,11 5,12 5,13 5,14 5,15
4 5 6 7 8 9 10 11 12 13 14 15
4,5 4,6 4,7 4,8 4,9 4,10 4,11 4,12 4,13 4,14 6,7 6,8 6,9 6,10 6,11 6,12 6,13 6,14
7,9 7,10 7,11 7,12 7,13 7,14 7,15 9,11 9,12 9,13 9,14 9,15 11,13 11,14 11,15
8 9 10 11 12 13 14 15
8,9 8,10 8,11 8,12 8,13 8,14 10,11 10,12 10,13 10,14 12,13 12,14 13,14

FIG. 30

	4	5	6	7	8	9	10	11	12	13	14	15	X
1,2,3		X	X	X	X	X	X	X	X	X	X	X	2,3,4
1,2,4			X	X	X	X	X	X	X	X	X	X	2,3,5
1,2,5				X	X	X	X	X	X	X	X	X	2,3,6
1,2,6					X	X	X	X	X	X	X	X	2,3,7
1,2,7						X	X	X	X	X	X	X	2,3,8
1,2,8							X	X	X	X	X	X	2,3,9
1,2,9								X	X	X	X	X	2,3,10
1,2,10									X	X	X	X	2,3,11
1,2,11										X	X	X	2,3,12
1,2,12											X	X	2,3,13
1,2,13												X	2,3,14
1,2,14			X	X	X	X	X	X	X	X	X	X	2,4,5
1,3,4				X	X	X	X	X	X	X	X	X	2,4,6
1,3,5					X	X	X	X	X	X	X	X	2,4,7
1,3,6						X	X	X	X	X	X	X	2,4,8
1,3,7							X	X	X	X	X	X	2,4,9
1,3,8								X	X	X	X	X	2,4,10
1,3,9									X	X	X	X	2,4,11
1,3,10										X	X	X	2,4,12
1,3,11											X	X	2,4,13
1,3,12												X	2,4,14
1,3,13				X	X	X	X	X	X	X	X	X	2,5,6
1,3,14					X	X	X	X	X	X	X	X	2,5,7
1,4,5						X	X	X	X	X	X	X	2,5,8
1,4,6							X	X	X	X	X	X	2,5,9
1,4,7								X	X	X	X	X	2,5,10
1,4,8									X	X	X	X	2,5,11
1,4,9										X	X	X	2,5,12
1,4,10											X	X	2,5,13
1,4,11												X	2,5,14
1,4,12					X	X	X	X	X	X	X	X	2,6,7
1,4,13						X	X	X	X	X	X	X	2,6,8
1,4,14							X	X	X	X	X	X	2,6,9
1,5,6								X	X	X	X	X	2,6,10
1,5,7									X	X	X	X	2,6,11
1,5,8										X	X	X	2,6,12
1,5,9											X	X	2,6,13
1,5,10												X	2,6,14
1,5,11						X	X	X	X	X	X	X	2,7,8
1,5,12							X	X	X	X	X	X	2,7,9
1,5,13								X	X	X	X	X	2,7,10
1,5,14									X	X	X	X	2,7,11
1,6,7										X	X	X	2,7,12
1,6,8											X	X	2,7,13
1,6,9												X	2,7,14
1,6,10							X	X	X	X	X	X	2,8,9
1,6,11								X	X	X	X	X	2,8,10
1,6,12									X	X	X	X	2,8,11
1,6,13										X	X	X	2,8,12
1,6,14											X	X	2,8,13
1,7,8												X	2,8,14
1,7,9								X	X	X	X	X	2,9,10
1,7,10									X	X	X	X	2,9,11
1,7,11										X	X	X	2,9,12
1,7,12											X	X	2,9,13
1,7,13												X	2,9,14
1,7,14									X	X	X	X	2,10,11
1,8,9										X	X	X	2,10,12
1,8,10											X	X	2,10,13
1,8,11												X	2,10,14
1,8,12										X	X	X	2,11,12
1,8,13											X	X	2,11,13

	6	7	8	9	10	11	12	13	14	15	X
1,8,14										X	2,11,14
1,9,10									X	X	2,12,13
1,9,11										X	2,12,14
1,9,12										X	2,13,14
1,9,13	X	X	X	X	X	X	X	X	X	X	3,4,5
1,9,14		X	X	X	X	X	X	X	X	X	3,4,6
1,10,11			X	X	X	X	X	X	X	X	3,4,7
1,10,12				X	X	X	X	X	X	X	3,4,8
1,10,13					X	X	X	X	X	X	3,4,9
1,10,14						X	X	X	X	X	3,4,10
1,11,12							X	X	X	X	3,4,11
1,11,13								X	X	X	3,4,12
1,11,14									X	X	3,4,13
1,12,13										X	3,4,14
1,12,14	X	X	X	X	X	X	X	X	X	X	3,5,6
1,13,14		X	X	X	X	X	X	X	X	X	3,5,7
4,5,6			X	X	X	X	X	X	X	X	3,5,8
4,5,7				X	X	X	X	X	X	X	3,5,9
4,5,8					X	X	X	X	X	X	3,5,10
4,5,9						X	X	X	X	X	3,5,11
4,5,10							X	X	X	X	3,5,12
4,5,11								X	X	X	3,5,13
4,5,12									X	X	3,5,14
4,5,13			X	X	X	X	X	X	X	X	3,6,7
4,5,14				X	X	X	X	X	X	X	3,6,8
4,6,7					X	X	X	X	X	X	3,6,9
4,6,8						X	X	X	X	X	3,6,10
4,6,9							X	X	X	X	3,6,11
4,6,10								X	X	X	3,6,12
4,6,11									X	X	3,6,13
4,6,12										X	3,6,14
4,6,13					X	X	X	X	X	X	3,7,8
4,6,14						X	X	X	X	X	3,7,9
4,7,8							X	X	X	X	3,7,10
4,7,9								X	X	X	3,7,11
4,7,10									X	X	3,7,12
4,7,11										X	3,7,13
4,7,12										X	3,7,14
4,7,13					X	X	X	X	X	X	3,8,9
4,7,14							X	X	X	X	3,8,10
4,8,9								X	X	X	3,8,11
4,8,10									X	X	3,8,12
4,8,11										X	3,8,13
4,8,12										X	3,8,14
4,8,13						X	X	X	X	X	3,9,10
4,8,14							X	X	X	X	3,9,11
4,9,10								X	X	X	3,9,12
4,9,11									X	X	3,9,13
4,9,12										X	3,9,14
4,9,13							X	X	X	X	3,10,11
4,9,14								X	X	X	3,10,12
4,10,11									X	X	3,10,13
4,10,12										X	3,10,14
4,10,13								X	X	X	3,11,12
4,10,14									X	X	3,11,13
4,11,12										X	3,11,14
4,11,13									X	X	3,12,13
4,11,14										X	3,12,14
4,12,13										X	3,13,14
4,12,14			X	X	X	X	X	X	X	X	5,6,7
4,13,14				X	X	X	X	X	X	X	5,6,8
6,7,8					X	X	X	X	X	X	5,6,9

	9	10	11	12	13	14	15	X
6,7,9			X	X	X	X	X	5,6,10
6,7,10				X	X	X	X	5,6,11
6,7,11					X	X	X	5,6,12
6,7,12						X	X	5,6,13
6,7,13							X	5,6,14
6,7,14	X	X	X	X	X	X	X	5,7,8
6,8,9		X	X	X	X	X	X	5,7,9
6,8,10			X	X	X	X	X	5,7,10
6,8,11				X	X	X	X	5,7,11
6,8,12					X	X	X	5,7,12
6,8,13						X	X	5,7,13
6,8,14							X	5,7,14
6,9,10		X	X	X	X	X	X	5,8,9
6,9,11			X	X	X	X	X	5,8,10
6,9,12				X	X	X	X	5,8,11
6,9,13					X	X	X	5,8,12
6,9,14						X	X	5,8,13
6,10,11							X	5,8,14
6,10,12			X	X	X	X	X	5,9,10
6,10,13				X	X	X	X	5,9,11
6,10,14					X	X	X	5,9,12
6,11,12						X	X	5,9,13
6,11,13							X	5,9,14
6,11,14				X	X	X	X	5,10,11
6,12,13					X	X	X	5,10,12
6,12,14						X	X	5,10,13
6,13,14							X	5,10,14
7,8,9					X	X	X	5,11,12
7,8,10						X	X	5,11,13
7,8,11							X	5,11,14
7,8,12						X	X	5,12,13
7,8,13							X	5,12,14
7,8,14							X	5,13,14
7,9,10			X	X	X	X	X	8,9,10
7,9,11				X	X	X	X	8,9,11
7,9,12					X	X	X	8,9,12
7,9,13						X	X	8,9,13
7,9,14							X	8,9,14
7,10,11				X	X	X	X	8,10,11
7,10,12					X	X	X	8,10,12
7,10,13						X	X	8,10,13
7,10,14							X	8,10,14
7,11,12					X	X	X	8,11,12
7,11,13						X	X	8,11,13
7,11,14							X	8,11,14
7,12,13						X	X	8,12,13
7,12,14							X	8,12,14
7,13,14							X	8,13,14
9,10,11					X	X	X	10,11,12
9,10,12						X	X	10,11,13
9,10,13							X	10,11,14
9,10,14						X	X	10,12,13
9,11,12							X	10,12,14
9,11,13							X	10,13,14
9,11,14						X	X	11,12,13
9,12,13							X	11,12,14
9,12,14							X	11,13,14
9,13,14							X	12,13,14

FIG. 31

Well	Cell Tracker Dye		
	Pacific Blue	DiR	DiD
1	+	-	-
2	-	+	-
3	-	-	+

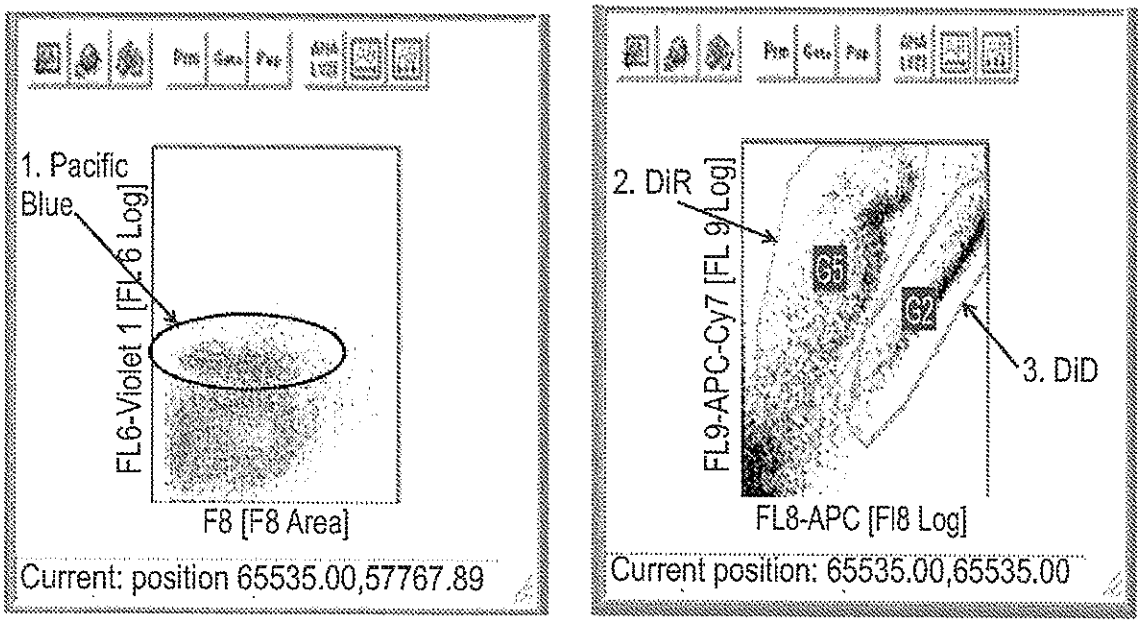


FIG. 32

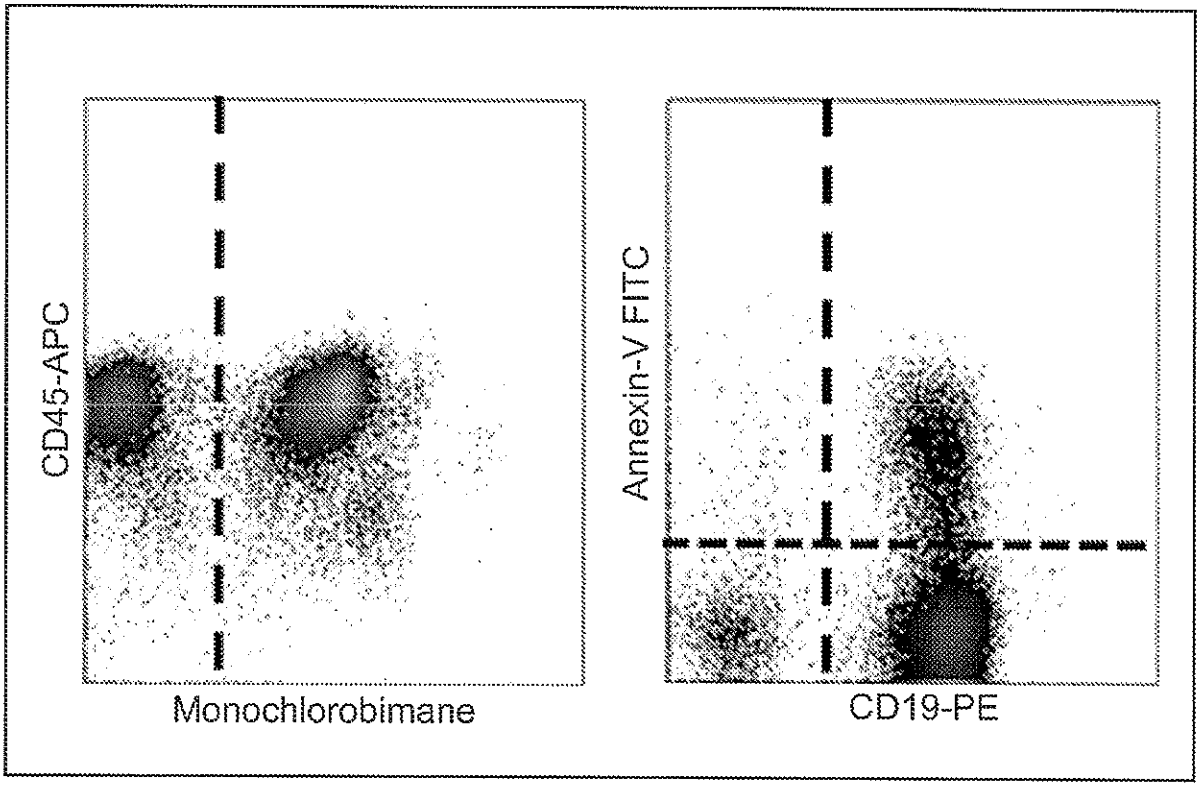


FIG. 33