

SEARCH FOR NEW DRUGS

ANTITUMOR ACTIVITY OF SOME POLYNITRILE DERIVATIVES

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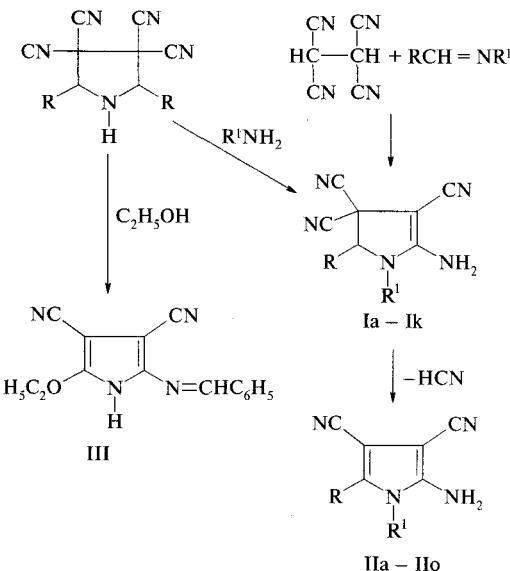
Investigation of the properties of organic polynitriles such as ethane-1,1,2,2-tetracarbonitrile and 4-oxoalkane-1,1,2,2-tetracarbonitriles made it possible to develop an approach to various classes of cyano-containing heterocyclic systems. Some of these compounds, possessing pesticide activity, were also found to be valuable products for further synthesis. For example, pyrroles with *o*-enaminonitrile fragments interact with formamide to form 4-amino-5-cyanopyrrolo[2,3-d]pyrimidines representing structural analogs of the natural nucleoside antitumor antibiotic toyocamycin [1, 2]. In connection with this, the purpose of our work was to study the antitumor activity of some cyano-containing heterocycles synthesized previously as described in [3–13].

The interaction of ethane-1,1,2,2-tetracarbonitrile with the Schiff bases led to 2-amino-5-R-1-R'-2-pyrroline-3,4,4-tricarbonitriles (Ia–If), while the reactions with aldehyde azines yielded the corresponding 1-ylideneaminopyrrolines (Ig–Ik). On heating in a high-boiling solvent, all pyrrolines I readily eliminate a hydrogen cyanide molecule with the formation of the corresponding pyrrole (IIa–IIo) [3–5].

Some of pyrrolines I were synthesized by reacting 2,5-disubstituted pyrrolidine-3,3,4,4-tetracarbonitriles [6] with amines [7], while the reaction with ethanol led to 2-benzylideneamino-5-ethoxypyrrrole-3,4-dicarbonitrile (III) [8].

The reactions of 4-oxoalkane-1,1,2,2-tetracarbonitriles (A) with aldehydes lead to 1,3,8-trisubstituted 6-imino-2,7-dioxabicyclo[3.2.1]octane-4,4,5-tricarbonitriles (IVa–IVn), which were previously assigned the structure of 5-imino-2,6-dioxabicyclo[2.2.2]octanes [9]. Compounds IV of higher purity can be obtained using 4-oxoalkane-1,1,2,2-tetracarbonitriles and 1,3,5-trisubstituted 2,4-diazapentane-1,4-dienes in aqueous acetic acid [10].

When acetone or 2-propanol are used as solvents, the interaction of tetracyanoalkanes (A) with 1,3,5-triaryl-2,4-diazapentane-1,4-dienes proceeds with the formation of 1,3,5-triaryl-9-oxo-1,2,3,4b,5,6,8a,9-octahydropyrido[3',4':3,4]-pyrrolo[1,2-a][1,3,5]triazine-4b,8a-dicarbonitriles (Va–Ve) [11].

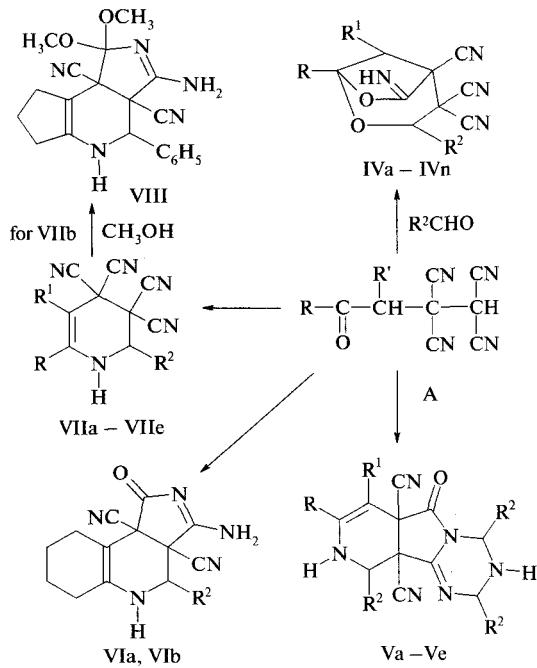


- I: a) $\text{R} = 3\text{-O}_2\text{NC}_6\text{H}_4$, $\text{R}' = 4\text{-H}_3\text{COOC}_6\text{H}_4$; b) $\text{R} = \text{C}_3\text{H}_7$,
 $\text{R}' = -\text{CH}_2\text{CH}=\text{CH}_2$; c) $\text{R} = 2\text{-furyl}$, $\text{R}' = \text{C}_6\text{H}_5$, d) $\text{R} = \text{R}' = \text{C}_6\text{H}_5$;
e) $\text{R} = \text{C}_6\text{H}_5$, $\text{R}' = 2\text{-H}_3\text{CC}_6\text{H}_4$; f) $\text{R} = \text{C}_6\text{H}_5$, $\text{R}' = 4\text{-H}_3\text{CC}_6\text{H}_4$; g)
 $\text{R} = \text{C}_2\text{H}_5$, $\text{R}' = -\text{N}=\text{CHC}_2\text{H}_5$; i) $\text{R} = \text{C}_6\text{H}_5$, $\text{R}' = -\text{N}=\text{CHC}_6\text{H}_5$; j)
 $\text{R} = i\text{-C}_3\text{H}_7$, $\text{R}' = -\text{N}-\text{CH}(\text{CH}_3)_2$; k) $\text{R} = 2\text{-furyl}$, $\text{R}' = -\text{N}-\text{CH-2-furyl}$;
II: a) $\text{R} = 3\text{-O}_2\text{NC}_6\text{H}_4$, $\text{R}' = 4\text{-H}_3\text{COOC}_6\text{H}_4$; b) $\text{R} = \text{C}_3\text{H}_7$,
 $\text{R}' = -\text{CH}_2\text{CH}=\text{CH}_2$; c) $\text{R} = 2\text{-furyl}$, $\text{R}' = \text{C}_6\text{H}_5$; d) $\text{R} = \text{R}' = \text{C}_6\text{H}_5$;
e) $\text{R} = i\text{-C}_4\text{H}_9$, $\text{R}' = \text{CH}_2\text{C}_6\text{H}_5$; f) $\text{R} = \text{C}_6\text{H}_5$, $\text{R}' = -\text{CH}_2\text{CH}=\text{CH}_2$;
g) $\text{R} = \text{C}_6\text{H}_5$, $\text{R}' = \text{CH}_2\text{C}_6\text{H}_5$; i) $\text{R} = \text{C}_6\text{H}_5$, $\text{R}' = 4\text{-H}_3\text{COOC}_6\text{H}_4$;
j) $\text{R} = 3\text{-O}_2\text{NC}_6\text{H}_4$, $\text{R}' = \text{C}_6\text{H}_5$; k) $\text{R} = 2\text{-furyl}$, $\text{R}' = 4\text{-H}_3\text{COOC}_6\text{H}_4$;
l) $\text{R} = \text{CH}_3$, $\text{R}' = -\text{N}-\text{CHCH}_3$; m) $\text{R} = i\text{-C}_3\text{H}_7$, $\text{R}' = -\text{N}=\text{CHC}_3\text{H}_7$;
n) $\text{R} = 2\text{-furyl}$, $\text{R}' = -\text{N}-\text{CH-2-furyl}$; o) $\text{R} = \text{C}_6\text{H}_5$, $\text{R}' = -\text{N}-\text{CHC}_6\text{H}_5$.

In some of these reactions, it is possible to isolate the intermediate products representing 3-amino-4-aryl-6,7-tetramethylene-1-oxo-3a,4,5,7a-tetrahydro-1H-pyrrolo[3,4-c]pyridine-3a,7a-dicarbonitriles (VIa, VIb) [11]. These compounds can be also obtained by isomerization of 2-aryl-5,6-tetramethylene-3,3,4-tricyano-2,3,4,5-tetrahydro-pyridine-4-carboxamides under the action of acids [12]. In glacial acetic acid, the reactions of alkanones (A) quantitatively yield tetrahydropyridines VIIa–VIIe [11], and the interaction of

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VIIb with methanol under mild conditions leads to 3-amino-6,7-trimethylene-1,1-dimethoxy-4-phenyl-3a,4,5,7a-tetrahydro-1H-pyrrolo[3,4-c]pyridine-3a,7a-dicarbonitrile (VIII) [13].



- IV: a) $R + R^1 = (\text{CH}_2)_4$, $R^2 = 2\text{-furyl}$; b) $R + R^1 = (\text{CH}_2)_4$, $R^2 = i\text{-C}_3\text{H}_7$;
 c) $R + R^1 = (\text{CH}_2)_4$, $R^2 = \text{CH}_3$; d) $R + R^1 = (\text{CH}_2)_4$, $R^2 = \text{H}$;
 e) $R = R^1 = \text{CH}_3$, $R^2 = 3\text{-O}_2\text{NC}_6\text{H}_4$; f) $R = R^1 = \text{CH}_3$, $R^2 = \text{C}_6\text{H}_5$;
 g) $R = R^1 = \text{CH}_3$, $R^2 = 2\text{-furyl}$; i) $R = R^1 = \text{CH}_3$, $R^2 = i\text{-C}_3\text{H}_7$;
 j) $R = R^1 = \text{CH}_3$; k) $R = R^1 = \text{CH}_3$, $R^2 = \text{H}$; l) $R = \text{CH}_3$, $R^1 = \text{H}$,
 $R^2 = \text{C}_2\text{H}_5$; m) $R = \text{CH}_3$, $R^1 = R^2 = \text{H}$; n) $R + R^1 = (\text{CH}_2)_4$, $R^2 = \text{C}_6\text{H}_5$;
 V: a) $R + R^1 = (\text{CH}_2)_4$, $R^2 = 2\text{-furyl}$; b) $R = R^1 = \text{CH}_3$, $R^2 = \text{C}_6\text{H}_5$;
 c) $R = R^1 = \text{CH}_3$, $R^2 = 2\text{-furyl}$; d) $R + R^1 = (\text{CH}_2)_4$, $R^2 = \text{C}_6\text{H}_5$;
 e) $R + R^1 = (\text{CH}_2)_3$, $R^2 = \text{C}_6\text{H}_5$;
 VI: a) $R^2 = 2\text{-furyl}$; b) $R^2 = 4\text{-H}_3\text{COOC}_6\text{H}_5$;
 VII: a) $R + R^1 = (-\text{CH}_2)_4$, $R^2 = 4\text{-BrC}_6\text{H}_4$; b) $R + R^1 = (-\text{CH}_2)_3$,
 $R^2 = \text{C}_6\text{H}_5$; c) $R = R^1 = \text{CH}_3$, $R^2 = \text{C}_6\text{H}_5$; d) $R = \text{CH}_3$, $R^1 = \text{H}$, $R^2 = \text{C}_6\text{H}_5$;
 e) $R + R^1 = (-\text{CH}_2)_4$, $R^2 = 2\text{-furyl}$.

EXPERIMENTAL BIOLOGICAL PART

The antitumor activity of the synthesized compounds was studied at the National Cancer Institute (Maryland, USA). The tests were performed on the same *in vitro* model that provided for standardization of the experimental conditions in repeating series. The experiments were conducted on 60 cell lines obtained from solid tumors of various human organs including lung (cell lines A549/ATCC, EKVVX, HOP-62, HOP-92, NCI-H226, NCI-H23, NCI-H322M, NCI-H460, NCI-H522), rectum (COLO 205, HCC-2998, HCT-116, HCT-15, HT-29, KM12, SW-620), brain (SF-268, SF-295, SF-539, SNB-75, SNB-19, U251), ovary (IGROV₁, OVCAR-3, OVCAR-4, OVCAR-5, OVCAR-8, SK-OV-3), kidney (786 - 0, A-498, ACHN, CAKI-1, RXF 393, SN12C,

TK-10, UO-31), prostate (PC-3, DU-145), and breast (MCF7, NCI/ADR-RES, MDA-MB-231/ATCC, HS 578T, MDA-MB-435, MDA-N, BT-549, T47D), as well as leukemia (CCRF-CEM, HL-60(TB), K-562, MOLT-4, RPMI-8226, SR), and melanoma (LOX IMVI, MALMB-3M, M-14, SK-MEL-2, SK-MEL-28, SK-MEL-5, UACC-257, UACC-62).

The cells were grown on a test plate with microwells with or without the synthesized compounds. The antitumor activity was manifested by inhibition of the tumor cell growth; the cell concentration was measured spectrophotometrically. The cell growth termination was determined using the pink anionic dye Sulforhodamine B (SRB), capable of attaching to the living cells modified by trichloroacetic acid. After the sample was washed, the bound dye was determined by spectrophotometry [14]. The analysis is based upon expected cytotoxic activity of the synthesized compounds with respect to the tumor cells.

The untreated tumor cells, as well as those treated with the tested compounds, were placed on a 96-well plate. Stock solutions of the synthesized compounds in DMSO were diluted to 1 : 200 with a cell culture medium. Further serial dilutions were performed (before adding to the cell cultures) so as to obtain the following molar concentrations: 10^{-8} , 10^{-7} , 10^{-6} , 10^{-5} , 10^{-4} (or from -8 to -4 with a unity step on the logarithmic scale). Cultures of the tumor cell lines with the serial dilutions of synthesized compounds were incubated for 48 h. Then the samples were fixed, washed, and dried. Finally, SRB was added and the cells were washed once again so as to ensure that the bound dye would pass into solution.

The effect of the synthesized compounds upon the tumor cell line was determined as percentage growth (PG) of the tumor cells calculated by the following formulas. If the average optical density of the dye (SRB) determined upon a 48-h exposure to the cells with a drug (D_{test}) is greater than or equal to the average value for the zero incubation time (D_0), so that $D_{\text{test}} - D_0 \geq 0$, then

$$PG = \frac{100(D_{\text{test}} - D_0)}{(D_{\text{contr}} - D_0)},$$

and for $D_{\text{test}} - D_0 < 0$,

$$PG = \frac{100(D_{\text{test}} - D_0)}{OD_0},$$

where D_{contr} is the average optical density of the dye determined upon the 48-h exposure with the tumor cells without inhibitors.

The results of screening are summarized in Table 1 showing variation of the optical density of each sample as a function of the drug concentration for various cell lines and variation of the PG value with the drug's concentration in each line. Also presented are the characteristic quantities

TABLE 1. Antitumor Activity of Polynitrile Derivatives

Panel/Cell Line		Compound/parameter											
1		Ia			Ib			Ic			Id		
2		GI ₅₀	TGI	LC ₅₀	GI ₅₀	TGI	LC ₅₀	GI ₅₀	TGI	LC ₅₀	GI ₅₀	TGI	LC ₅₀
Leukemia													
3	CCPF-CEM	2.68 ^c	6.06 ^c	7.88 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.43 ^b	4.39 ^b	> 1.00 ^a	1.28 ^b	3.37 ^b	8.88 ^b
4	HL-60(TB)	3.00 ^c	6.58 ^c	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.76 ^b	5.34 ^b	> 1.00 ^a	1.70 ^b	4.39 ^b	> 1.00 ^a
5	K-562	2.92 ^c	1.47 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	6.57 ^c	3.75 ^b	> 1.00 ^a	6.05 ^b	2.65 ^b	9.02 ^b
6	MOLT-4	2.77 ^c	7.03 ^c	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	2.55 ^b	7.10 ^b	> 1.00 ^a	1.23 ^b	3.17 ^b	8.13 ^b
7	RPMI-8226	1.01 ^b	3.56 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.94 ^b	4.55 ^b	> 1.00 ^a	1.48 ^b	3.70 ^b	9.28 ^b
8	SR	1.44 ^b	4.36 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	2.05 ^b	5.11 ^b	> 1.00 ^a	1.71 ^b	4.05 ^b	9.58 ^b
Large-cell lung carcinoma													
9	A549/ATCC	1.96 ^b	3.72 ^b	7.05 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	3.82 ^b	> 1.00 ^a	> 1.00 ^a	1.78 ^b	4.52 ^b	> 1.00 ^a
10	EKVX	2.21 ^b	4.30 ^b	8.37 ^b	4.75 ^b	> 1.00 ^a	> 1.00 ^a	2.00 ^b	7.33 ^b	> 1.00 ^a	1.97 ^b	4.38 ^b	9.73 ^b
11	HOP-62	1.57 ^b	3.13 ^b	6.22 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	2.18 ^b	5.43 ^b	> 1.00 ^a	1.80 ^b	3.68 ^b	7.53 ^b
12	NCI-H226	1.95 ^b	3.43 ^b	6.01 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.80 ^b	4.20 ^b	9.79 ^b	1.77 ^b	3.62 ^b	7.38 ^b
13	NCI-H23	1.86 ^b	3.65 ^b	7.16 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.99 ^b	3.89 ^b	7.61 ^b	2.08 ^b	4.48 ^b	9.62 ^b
14	NCI-H322M	1.83 ^b	3.24 ^b	5.72 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.95 ^b	4.18 ^b	8.98 ^b	1.97 ^b	3.94 ^b	7.88 ^b
15	NCI-H522	3.18 ^c	1.35 ^b	4.55 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.68 ^b	3.52 ^b	7.40 ^b	1.63 ^b	3.49 ^b	7.47 ^b
Cancer of the intestine													
16	COLO 205	1.12 ^b	2.52 ^b	5.65 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.93 ^b	3.92 ^b	7.94 ^b	1.72 ^b	3.61 ^b	7.60 ^b
17	HCC-2998	1.71 ^b	3.32 ^b	6.44 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.64 ^b	3.13 ^b	6.00 ^b	1.64 ^b	3.02 ^b	5.54 ^b
18	HCT-116	7.48 ^c	2.10 ^b	4.97 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	2.85 ^b	> 1.00 ^a	> 1.00 ^a	1.44 ^b	2.94 ^b	5.98 ^b
19	HCT-15	1.29 ^b	2.66 ^b	5.48 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.83 ^b	4.32 ^b	> 1.00 ^a	2.06 ^b	5.11 ^b	> 1.00 ^a
20	HT29	1.24 ^b	2.66 ^b	5.68 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	2.00 ^b	3.71 ^b	6.90 ^b	1.57 ^b	3.02 ^b	5.83 ^b
21	KM12	1.89 ^b	3.44 ^b	6.25 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.74 ^b	3.72 ^b	7.95 ^b	1.45 ^b	3.09 ^b	6.59 ^b
22	SW-620	8.27 ^c	2.23 ^b	5.30 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.79 ^b	3.92 ^b	8.55 ^b	1.91 ^b	3.72 ^b	7.25 ^b
Brain cancer													
23	SF-268	2.07 ^b	4.31 ^b	8.98 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	3.47 ^b	> 1.00 ^a	> 1.00 ^a	2.27 ^b	5.54 ^b	> 1.00 ^a
24	CF-295	1.89 ^b	4.01 ^b	8.49 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	2.84 ^b	9.39 ^b	> 1.00 ^a	1.84 ^b	6.11 ^b	> 1.00 ^a
25	CF-539	1.28 ^b	2.70 ^b	5.70 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.93 ^b	4.12 ^b	8.78 ^b	1.47 ^b	3.25 ^b	7.19 ^b
26	SNB-19	1.92 ^b	3.40 ^b	6.05 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	2.69 ^b	7.14 ^b	> 1.00 ^a	1.83 ^b	4.32 ^b	> 1.00 ^a
27	SNB-75	1.58 ^b	3.04 ^b	5.85 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	2.00 ^b	6.68 ^b	> 1.00 ^a	1.53 ^b	4.20 ^b	> 1.00 ^a
28	U ₂ 51	1.73 ^b	3.15 ^b	5.74 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	2.18 ^b	4.30 ^b	8.49 ^b	1.71 ^b	3.24 ^b	6.15 ^b
Melanoma													
29	LOX IMVI	1.25 ^b	2.64 ^b	5.59 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.67 ^b	3.11 ^b	5.80 ^b	1.66 ^b	3.03 ^b	5.51 ^b
30	MALME-3M	2.64 ^c	7.91 ^c	2.96 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	2.29 ^b	5.28 ^b	> 1.00 ^a	1.76 ^b	3.56 ^b	7.20 ^b
31	M ₁₄	1.90 ^b	4.24 ^b	9.47 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	2.06 ^b	4.34 ^b	9.12 ^b	2.11 ^b	4.49 ^b	9.58 ^b
32	SK-MEL-2	1.91 ^b	3.55 ^b	6.61 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	2.75 ^b	5.94 ^b	> 1.00 ^a	1.65 ^b	4.29 ^b	> 1.00 ^a
33	SK-MEL-28	4.59 ^c	1.78 ^b	4.54 ^b	—	—	—	1.79 ^b	3.89 ^b	8.43 ^b	1.67 ^b	3.11 ^b	5.80 ^b
34	CK-MEL-5	1.26 ^b	2.59 ^b	5.31 ^b	8.17 ^b	> 1.00 ^a	> 1.00 ^a	1.74 ^b	3.23 ^b	6.00 ^b	1.35 ^b	2.69 ^b	5.35 ^b
35	UAC-257	1.28 ^b	2.70 ^b	5.72 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.84 ^b	3.72 ^b	7.53 ^b	1.91 ^b	3.49 ^b	6.39 ^b
36	UAC-62	1.47 ^b	2.86 ^b	5.56 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	2.32 ^b	5.93 ^b	> 1.00 ^a	1.83 ^b	4.57 ^b	> 1.00 ^a
Ovarian cancer													
37	IGROV ₁	1.13 ^b	2.48 ^b	5.43 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.92 ^b	4.79 ^b	> 1.00 ^a	1.57 ^b	3.20 ^b	6.52 ^b
38	OVCAR-3	1.47 ^b	3.06 ^b	6.37 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.90 ^b	5.66 ^b	> 1.00 ^a	1.78 ^b	3.46 ^b	6.71 ^b
39	OVCAR-4	1.64 ^b	3.04 ^b	5.63 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	2.13 ^b	4.90 ^b	> 1.00 ^a	1.96 ^b	5.11 ^b	> 1.00 ^a
40	OVCAR-5	1.89 ^b	3.95 ^b	8.26 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	2.29 ^b	4.84 ^b	> 1.00 ^a	1.61 ^b	3.73 ^b	8.66 ^b
41	OVCAR-8	1.89 ^b	3.32 ^b	5.85 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	2.33 ^b	5.18 ^b	> 1.00 ^a	1.62 ^b	3.35 ^b	6.93 ^b
42	SK-OV-3	2.12 ^b	3.76 ^b	6.67 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	7.78 ^b	1.00 ^a	> 1.00 ^a	2.49 ^b	7.84 ^b	> 1.00 ^a
Renal cancer													
43	786-0	1.38 ^b	2.84 ^b	5.84 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.75 ^b	3.51 ^b	7.05 ^b	1.75 ^b	3.26 ^b	6.05 ^b
44	A498	1.62 ^b	2.99 ^b	5.55 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	2.18 ^b	4.91 ^b	> 1.00 ^a	1.74 ^b	3.36 ^b	6.52 ^b
45	ACHN	1.25 ^b	2.50 ^b	5.00 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.67 ^b	3.20 ^b	6.14 ^b	1.81 ^b	4.07 ^b	9.17 ^b

46	CAKI-1	1.41 ^b	3.05 ^b	6.57 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	3.06 ^b	> 1.00 ^a	> 1.00 ^a	2.09 ^b	> 1.00 ^a	> 1.00 ^a
47	RXF 393	5.66 ^c	1.96 ^b	5.12 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.75 ^b	3.71 ^b	7.89 ^b	1.50 ^b	3.36 ^b	7.56 ^b
48	SN12C	1.47 ^b	2.94 ^b	5.90 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	3.03 ^b	1.00 ^a	1.00 ^a	1.89 ^b	3.66 ^b	7.09 ^b
49	TK-10	1.39 ^b	2.75 ^b	5.44 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.64 ^b	3.15 ^b	6.04 ^b	1.65 ^b	3.18 ^b	6.14 ^b
50	UO-31	1.72 ^b	3.15 ^b	5.74 ^b	7.52 ^b	> 1.00 ^a	> 1.00 ^a	1.87 ^b	3.36 ^b	6.02 ^b	1.81 ^b	3.48 ^b	6.70 ^b
Cancer of the prostate													
51	PC-3	1.83 ^b	3.55 ^b	6.89 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	2.74 ^b	6.05 ^b	1.00 ^a	1.77 ^b	4.03 ^b	9.20 ^b
52	DU-145	1.82 ^b	3.23 ^b	5.73 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.94 ^b	3.74 ^b	7.21 ^b	1.78 ^b	3.29 ^b	6.08 ^b
Breast cancer													
53	MCF7	2.33 ^b	5.06 ^b	> 6.89 ^a	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.74 ^b	4.39 ^b	1.00 ^a	1.48 ^b	3.17 ^b	6.79 ^b
54	MCF7/ADR-RES	2.26 ^b	4.74 ^b	9.94 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	2.70 ^b	5.62 ^b	1.00 ^a	2.03 ^b	4.53 ^b	> 1.00 ^a
55	MDA-MB-231/ATC	1.36 ^b	2.80 ^b	5.75 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.53 ^b	3.51 ^b	8.05 ^b	1.43 ^b	2.98 ^b	6.19 ^b
56	HS 578T	2.09 ^b	5.17 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	3.65 ^b	> 1.00 ^a	> 1.00 ^a	3.00 ^b	> 1.00 ^a	> 1.00 ^a
57	MDA-MB-435	1.70 ^b	3.14 ^b	5.81 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	2.84 ^b	7.18 ^b	> 1.00 ^a	1.88 ^b	3.56 ^b	6.74 ^b
58	MDA-N	1.70 ^b	3.13 ^b	5.74 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	2.78 ^b	> 1.00 ^a	> 1.00 ^a	1.93 ^b	4.10 ^b	8.72 ^b
59	BT-549	1.80 ^b	3.23 ^b	5.83 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.88 ^b	3.74 ^b	7.45 ^b	1.67 ^b	3.70 ^b	8.16 ^b
60	T-47D	1.39 ^b	3.20 ^b	7.38 ^b	5.49 ^b	> 1.00 ^a	> 1.00 ^a	1.52 ^b	8.10 ^b	1.00 ^a	1.04 ^b	2.44 ^b	5.74 ^b

	Ie			If			Ig			Ii			Ij		
	GI ₅₀	TGI	LC ₅₀	GI ₅₀	TGI	LC ₅₀	GI ₅₀	TGI	LC ₅₀	GI ₅₀	TGI	LC ₅₀	GI ₅₀	TGI	LC ₅₀
3	1.47 ^b	3.67 ^b	9.20 ^b	3.00 ^c	7.33 ^c	5.69 ^b	3.60 ^b	> 1.00 ^a	> 1.00 ^a	1.72 ^c	5.29 ^c	7.35 ^b	3.62 ^b	9.32 ^b	> 1.00 ^a
4	1.85 ^b	4.42 ^b	> 1.00 ^a	2.75 ^c	6.15 ^c	6.60 ^b	3.58 ^b	8.56 ^b	> 1.00 ^a	3.02 ^c	7.18 ^c	> 1.00 ^a	3.24 ^b	9.17 ^b	> 1.00 ^a
5	—	—	—	—	—	—	5.27 ^b	> 1.00 ^a	> 1.00 ^a	2.72 ^c	6.76 ^c	> 1.00 ^a	4.20 ^b	> 1.00 ^a	> 1.00 ^a
6	1.56 ^b	3.93 ^b	9.90 ^b	2.31 ^c	8.27 ^c	6.10 ^b	3.90 ^b	> 1.00 ^a	> 1.00 ^a	1.90 ^c	5.01 ^c	> 1.00 ^a	3.48 ^b	> 1.00 ^a	> 1.00 ^a
7	1.92 ^b	4.52 ^b	> 1.00 ^a	1.14 ^b	3.21 ^b	9.02 ^b	8.30 ^b	> 1.00 ^a	> 1.00 ^a	2.20 ^c	5.50 ^c	7.93 ^b	3.78 ^b	> 1.00 ^a	> 1.00 ^a
8	2.39 ^b	6.04 ^b	> 1.00 ^a	8.66 ^c	3.37 ^b	> 1.00 ^a	3.47 ^b	> 1.00 ^a	> 1.00 ^a	2.49 ^c	1.28 ^b	7.52 ^b	2.93 ^b	8.28 ^b	> 1.00 ^a
9	2.61 ^b	6.27 ^b	> 1.00 ^a	1.67 ^b	3.82 ^b	8.78 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.55 ^b	3.24 ^b	6.77 ^b	6.04 ^b	> 1.00 ^a	> 1.00 ^a
10	1.79 ^b	4.28 ^b	> 1.00 ^a	1.80 ^b	4.60 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	2.14 ^b	4.19 ^b	8.23 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a
11	1.94 ^b	4.24 ^b	9.31 ^b	1.95 ^b	3.69 ^b	7.01 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.57 ^b	3.09 ^b	6.05 ^b	5.57 ^b	> 1.00 ^a	> 1.00 ^a
HOP-92	1.38 ^b	3.58 ^b	9.30 ^b	7.79 ^c	2.18 ^b	5.43 ^b	—	—	—	—	—	—	—	—	—
12	2.07 ^b	3.88 ^b	7.27 ^b	1.96 ^b	3.89 ^b	7.74 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.78 ^b	3.33 ^b	6.24 ^b	5.56 ^b	> 1.00 ^a	> 1.00 ^a
13	1.94 ^b	3.86 ^b	7.66 ^b	1.81 ^b	3.81 ^b	8.03 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.70 ^b	3.32 ^b	6.45 ^b	6.49 ^b	> 1.00 ^a	> 1.00 ^a
14	1.95 ^b	3.66 ^b	6.85 ^b	1.83 ^b	3.33 ^b	6.05 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.78 ^b	3.16 ^b	5.62 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a
15	1.53 ^b	3.21 ^b	6.71 ^b	5.42 ^c	2.15 ^b	6.78 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	4.32 ^c	1.79 ^b	5.49 ^b	6.21 ^b	> 1.00 ^a	> 1.00 ^a
16	1.79 ^b	3.34 ^b	6.25 ^b	1.02 ^b	2.40 ^b	5.65 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	3.07 ^c	7.99 ^c	8.33 ^b	4.80 ^b	> 1.00 ^a	> 1.00 ^a
17	1.68 ^b	3.24 ^b	6.22 ^b	1.30 ^b	2.58 ^b	5.14 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.79 ^b	3.18 ^b	5.64 ^b	3.44 ^b	> 1.00 ^a	> 1.00 ^a
18	1.80 ^b	3.36 ^b	6.27 ^b	3.79 ^c	1.44 ^b	4.38 ^b	1.08 ^b	> 1.00 ^a	> 1.00 ^a	1.92 ^c	4.15 ^c	8.95 ^c	4.79 ^b	> 1.00 ^a	> 1.00 ^a
19	1.66 ^b	3.59 ^b	7.77 ^b	6.71 ^c	2.26 ^b	6.51 ^b	5.42 ^b	> 1.00 ^a	> 1.00 ^a	3.18 ^c	1.10 ^b	4.03 ^b	3.27 ^b	> 1.00 ^a	> 1.00 ^a
20	1.84 ^b	3.42 ^b	6.36 ^b	3.97 ^c	1.39 ^b	3.91 ^b	2.89 ^b	8.64 ^b	> 1.00 ^a	2.56 ^c	8.64 ^c	4.50 ^b	2.75 ^b	8.00 ^b	> 1.00 ^a
21	1.68 ^b	3.26 ^b	6.33 ^b	1.72 ^b	3.36 ^b	6.54 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.78 ^b	3.39 ^b	6.44 ^b	4.46 ^b	> 1.00 ^a	> 1.00 ^a
22	1.63 ^b	3.17 ^b	6.18 ^b	4.32 ^c	1.52 ^b	4.78 ^b	6.16 ^b	> 1.00 ^a	> 1.00 ^a	2.10 ^c	4.33 ^c	8.90 ^c	3.46 ^b	> 1.00 ^a	> 1.00 ^a
23	2, 10 ^b	4.57 ^b	9.98 ^b	2.49 ^b	6.59 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	2.38 ^b	6.06 ^b	> 1.00 ^a	5.67 ^b	> 1.00 ^a	> 1.00 ^a
24	2.47 ^b	6.89 ^b	> 1.00 ^a	1.89 ^b	6.03 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.57 ^b	3.84 ^b	9.41 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a
25	2.12 ^b	3.79 ^b	6.78 ^b	1.42 ^b	2.92 ^b	5.99 ^b	2.63 ^b	8.08 ^b	> 1.00 ^a	1.72 ^b	3.51 ^b	7.17 ^b	2.27 ^b	6.48 ^b	> 1.00 ^a
26	1.99 ^b	4.12 ^b	8.51 ^b	1.75 ^b	3.45 ^b	6.79 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.62 ^b	2.98 ^b	5.46 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a
27	2.60 ^b	4.60 ^b	8.14 ^b	1.32 ^b	2.80 ^b	5.95 ^b	8.18 ^b	> 1.00 ^a	> 1.00 ^a	1.60 ^b	2.99 ^b	5.59 ^b	4.27 ^b	> 1.00 ^a	> 1.00 ^a
28	1.67 ^b	3.19 ^b	6.06 ^b	1.73 ^b	3.16 ^b	5.78 ^b	5.86 ^b	> 1.00 ^a	> 1.00 ^a	1.63 ^b	2.99 ^b	5.47 ^b	3.96 ^b	> 1.00 ^a	> 1.00 ^a
29	1.77 ^b	3.27 ^b	6.01 ^b	1.15 ^b	2.39 ^b	4.95 ^b	4.89 ^b	> 1.00 ^a	> 1.00 ^a	5.62 ^c	1.91 ^b	5.05 ^b	3.18 ^b	> 1.00 ^a	> 1.00 ^a
30	1.64 ^b	3.26 ^b	6.46 ^b	1.15 ^b	2.78 ^b	6.70 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	2.06 ^c	4.44 ^c	9.58 ^c	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a
31	2.34 ^b	4.50 ^b	8.65 ^b	1.23 ^b	3.05 ^b	7.58 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.35 ^b	3.61 ^b	9.69 ^b	6.61 ^b	> 1.00 ^a	> 1.00 ^a
32	2.59 ^b	5.53<													

33	1.76 ^b	3.65 ^b	7.59 ^b	1.01 ^b	2.23 ^b	4.96 ^b	5.62 ^b	> 1.00 ^a	> 1.00 ^a	2.01 ^c	3.85 ^c	7.39 ^c	4.70 ^b	> 1.00 ^a	> 1.00 ^a	
34	1.59 ^b	3.01 ^b	5.70 ^b	8.63 ^c	2.09 ^b	4.57 ^b	5.31 ^b	> 1.00 ^a	> 1.00 ^a	9.70 ^c	2.14 ^b	4.63 ^b	3.83 ^b	> 1.00 ^a	> 1.00 ^a	
35	1.70 ^b	3.20 ^b	6.00 ^b	1.56 ^b	3.04 ^b	5.91 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.35 ^b	2.76 ^b	5.29 ^b	4.75 ^b	> 1.00 ^a	> 1.00 ^a	
36	1.79 ^b	3.77 ^b	7.93 ^b	1.13 ^b	2.67 ^b	6.27 ^b	5.95 ^b	> 1.00 ^a	> 1.00 ^a	1.32 ^b	3.03 ^b	6.98 ^b	2.64 ^b	7.65 ^b	> 1.00 ^a	
37	1.79 ^b	3.39 ^b	6.42 ^b	6.66 ^c	2.02 ^b	4.69 ^b	6.31 ^b	> 1.00 ^a	> 1.00 ^a	9.06 ^c	2.13 ^b	4.64 ^b	3.99 ^b	> 1.00 ^a	> 1.00 ^a	
38	1.72 ^b	3.56 ^b	7.39 ^b	1.37 ^b	2.74 ^b	5.48 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	2.88 ^c	1.01 ^b	3.24 ^b	4.82 ^b	> 1.00 ^a	> 1.00 ^a	
39	1.90 ^b	4.09 ^b	8.79 ^b	1.34 ^b	2.69 ^b	5.42 ^b	9.12 ^b	> 1.00 ^a	> 1.00 ^a	1.42 ^b	2.74 ^b	5.26 ^b	5.21 ^b	> 1.00 ^a	> 1.00 ^a	
40	2.19 ^b	4.15 ^b	7.86 ^b	1.55 ^b	3.23 ^b	6.75 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.80 ^b	3.73 ^b	7.71 ^b	5.03 ^b	> 1.00 ^a	> 1.00 ^a	
41	2.10 ^b	3.84 ^b	7.04 ^b	2.00 ^b	4.02 ^b	8.10 ^b	4.49 ^b	> 1.00 ^a	> 1.00 ^a	1.87 ^b	3.58 ^b	6.87 ^b	2.51 ^b	5.81 ^b	> 1.00 ^a	
42	3.13 ^b	8.66 ^b	> 1.00 ^a	1.67 ^b	4.76 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.37 ^b	2.79 ^b	5.68 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	
43	1.73 ^b	3.23 ^b	6.05 ^b	1.42 ^b	3.03 ^b	6.46 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	6.18 ^c	1.93 ^b	4.54 ^b	6.06 ^b	> 1.00 ^a	> 1.00 ^a	
44	1.66 ^b	3.37 ^b	6.83 ^b	1.70 ^b	3.57 ^b	7.52 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.59 ^b	2.93 ^b	5.42 ^b	5.12 ^b	> 1.00 ^a	> 1.00 ^a	
45	1.61 ^b	3.51 ^b	7.63 ^b	1.42 ^b	2.82 ^b	5.59 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	4.07 ^c	1.47 ^b	3.83 ^b	6.53 ^b	> 1.00 ^a	> 1.00 ^a	
46	2.59 ^b	> 1.00 ^a	> 1.00 ^a	8.98 ^c	3.09 ^b	9.76 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	8.42 ^c	2.07 ^b	4.55 ^b	8.51 ^b	> 1.00 ^a	> 1.00 ^a	
47	1.54 ^b	3.39 ^b	7.50 ^b	6.64 ^c	2.53 ^b	7.52 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	2.10 ^c	4.27 ^c	8.70 ^c	1.72 ^b	> 1.00 ^a	> 1.00 ^a	
48	2.33 ^b	5.90 ^b	> 1.00 ^a	1.44 ^b	3.09 ^b	6.63 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.27 ^b	2.95 ^b	6.88 ^b	6.98 ^b	> 1.00 ^a	> 1.00 ^a	
49	1.46 ^b	2.84 ^b	5.52 ^b	1.44 ^b	2.80 ^b	5.45 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.19 ^b	2.41 ^b	4.91 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	
50	1.68 ^b	3.12 ^b	5.78 ^b	1.59 ^b	3.20 ^b	6.46 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.57 ^b	3.02 ^b	5.83 ^b	3.81 ^b	> 1.00 ^a	> 1.00 ^a	
51	2.46 ^b	5.10 ^b	> 1.00 ^a	1.88 ^b	4.49 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.73 ^b	3.84 ^b	8.55 ^b	5.54 ^b	> 1.00 ^a	> 1.00 ^a	
52	1.67 ^b	3.08 ^b	5.67 ^b	1.49 ^b	2.82 ^b	5.35 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.51 ^b	2.86 ^b	5.43 ^b	4.00 ^b	> 1.00 ^a	> 1.00 ^a	
53	2.36 ^b	4.26 ^b	7.70 ^b	4.96 ^c	1.88 ^b	6.01 ^b	3.64 ^b	> 1.00 ^a	> 1.00 ^a	8.26 ^c	3.07 ^b	> 1.00 ^a	5.55 ^b	> 1.00 ^a	> 1.00 ^a	
54	2.07 ^b	4.22 ^b	8.57 ^b	1.70 ^b	3.61 ^b	7.64 ^b	9.21 ^b	> 1.00 ^a	> 1.00 ^a	2.30 ^b	6.22 ^b	> 1.00 ^a	3.12 ^b	8.28 ^b	> 1.00 ^a	
55	1.33 ^b	3.08 ^b	7.13 ^b	1.15 ^b	2.52 ^b	5.54 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.67 ^b	3.13 ^b	5.85 ^b	2.99 ^b	> 1.00 ^a	> 1.00 ^a	
56	2.01 ^b	5.81 ^b	> 1.00 ^a	2.10 ^b	7.67 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	2.40 ^b	6.75 ^b	> 1.00 ^a	8.86 ^b	> 1.00 ^a	> 1.00 ^a	
57	1.77 ^b	3.54 ^b	7.08 ^b	4.03 ^c	1.41 ^b	4.01 ^b	5.06 ^b	> 1.00 ^a	> 1.00 ^a	1.76 ^b	3.16 ^b	5.66 ^b	2.34 ^b	5.86 ^b	> 1.00 ^a	
58	1.71 ^b	3.82 ^b	8.52 ^b	3.09 ^c	1.20 ^b	4.23 ^b	5.35 ^b	> 1.00 ^a	> 1.00 ^a	1.40 ^b	2.73 ^b	5.30 ^b	2.25 ^b	6.98 ^b	> 1.00 ^a	
59	1.36 ^b	2.88 ^b	6.10 ^b	1.02 ^b	2.35 ^b	5.41 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.53 ^b	2.87 ^b	5.37 ^b	3.51 ^b	9.23 ^b	> 1.00 ^a	
60	1.25 ^b	3.10 ^b	7.65 ^b	5.74 ^c	2.14 ^b	5.72 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.17 ^b	3.84 ^b	> 1.00 ^a	4.88 ^b	> 1.00 ^a	> 1.00 ^a	
1	Ik				IIa				IIb				IIc			
2	GI ₅₀	TGI	LC ₅₀	GI ₅₀	TGI	LC ₅₀	GI ₅₀	TGI	LC ₅₀	GI ₅₀	TGI	LC ₅₀	GI ₅₀	TGI	LC ₅₀	
3	4.76 ^c	1.92 ^b	8.86 ^b	5.31 ^c	> 1.00 ^a	8.74 ^b	> 1.00 ^a	> 1.00 ^a								
4	3.35 ^c	7.69 ^b	> 1.00 ^a													
5	5.70 ^c	8.51 ^b	> 1.00 ^a	1.97 ^b	> 1.00 ^a	> 1.00 ^a										
6	1.19 ^b	3.03 ^b	7.70 ^b	2.46 ^c	4.48 ^b	> 1.00 ^a	4.31 ^b	> 1.00 ^a	6.03 ^b	> 1.00 ^a	> 1.00 ^a					
7	2.08 ^b	4.40 ^b	9.13 ^b	5.37 ^c	> 1.00 ^a	5.87 ^b	> 1.00 ^a	> 1.00 ^a								
8	1.60 ^b	3.93 ^b	9.64 ^b	1.88 ^b	> 1.00 ^a	> 1.00	2.25 ^b	> 1.00 ^a	> 1.00 ^a	9.82 ^b	> 1.00 ^a	> 1.00 ^a	7.37 ^b	> 1.00 ^a	> 1.00 ^a	
9	1.96 ^b	5.62 ^b	> 1.00 ^a	1.53 ^c	6.87 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	5.91 ^b	> 1.00 ^a	> 1.00 ^a	1.00 ^a	> 1.00 ^a	> 1.00 ^a	
10	1.95 ^b	4.73 ^b	> 1.00 ^a	2.60 ^b	> 1.00 ^a	> 1.00 ^a	4.26 ^b	> 1.00 ^a	> 1.00 ^a	4.50 ^b	> 1.00 ^a	> 1.00 ^a	7.38 ^b	> 1.00 ^a	> 1.00 ^a	
11	2.32 ^b	5.11 ^b	> 1.00 ^a	6.47 ^b	> 1.00 ^a	> 1.00 ^a	4.00 ^b	> 1.00 ^a	> 1.00 ^a	4.98 ^b	> 1.00 ^a	> 1.00 ^a	8.70 ^b	> 1.00 ^a	> 1.00 ^a	
HOP-92	1.66 ^b	3.35 ^b	6.76 ^b	1.53 ^b	> 1.00 ^a	> 1.00 ^a	4.00 ^b	> 1.00 ^a	> 1.00 ^a	4.98 ^b	> 1.00 ^a	> 1.00 ^a	—	—	—	
12	1.86 ^b	3.77 ^b	7.63 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	2.95 ^b	> 1.00 ^a	> 1.00 ^a	2.95 ^b	> 1.00 ^a	> 1.00 ^a	7.25 ^b	> 1.00 ^a	> 1.00 ^a	
13	1.96 ^b	3.58 ^b	6.55 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	2.95 ^b	> 1.00 ^a	> 1.00 ^a	2.95 ^b	> 1.00 ^a	> 1.00 ^a	8.06 ^b	> 1.00 ^a	> 1.00 ^a	
14	1.69 ^b	3.34 ^b	6.60 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	2.95 ^b	> 1.00 ^a	> 1.00 ^a	2.95 ^b	> 1.00 ^a	> 1.00 ^a	4.19 ^b	> 1.00 ^a	> 1.00 ^a	
15	1.53 ^b	3.11 ^b	6.13 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	2.95 ^b	> 1.00 ^a	> 1.00 ^a	2.95 ^b	> 1.00 ^a	> 1.00 ^a	4.19 ^b	> 1.00 ^a	> 1.00 ^a	
16	1.42 ^b	2.89 ^b	5.86 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	2.95 ^b	> 1.00 ^a	> 1.00 ^a	2.95 ^b	> 1.00 ^a	> 1.00 ^a	1.00 ^a	> 1.00 ^a	> 1.00 ^a	
17	1.94 ^b	3.47 ^b	6.19 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	2.95 ^b	> 1.00 ^a	> 1.00 ^a	2.95 ^b	> 1.00 ^a	> 1.00 ^a	5.51 ^c	> 1.00 ^a	> 1.00 ^a	
18	1.27 ^b	2.53 ^b	5.03 ^b	—	—	—	—	> 1.00 ^a	> 1.00 ^a	2.95 ^b	> 1.00 ^a	> 1.00 ^a				

56	> 1.00 ^a	2.56 ^b	> 1.00 ^a	> 1.00 ^a	6.58 ^c	> 1.00 ^a	> 1.00 ^a	5.51 ^b	> 1.00 ^a	> 1.00 ^a					
57	> 1.00 ^a														
58	> 1.00 ^a	—	> 1.00 ^a												
59	> 1.00 ^a	> 100 ^a	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.91 ^b	> 1.00 ^a	> 1.00 ^a	5.11 ^c	> 1.00 ^a	> 1.00 ^a
60	> 1.00 ^a	4.57 ^c	> 1.00 ^a												
1	IIk			III			IIIm			IIIn			IIO		
2	GI ₅₀	TGI	LC ₅₀	GI ₅₀	TGI	LC ₅₀	GI ₅₀	TGI	LC ₅₀	GT ₅₀	TGI	LC ₅₀	GI ₅₀	TGI	LC ₅₀
3	> 1.00 ^a	1.99 ^b	> 1.00 ^a	1.23 ^b	5.12 ^b	> 1.00 ^a									
4	> 1.00 ^a	2.61 ^b	> 1.00 ^a	1.61 ^b	> 1.00 ^a	> 1.00 ^a									
5	5.97 ^b	> 1.00 ^a	2.40 ^b	> 1.00 ^a	1.32 ^b	> 1.00 ^a	> 1.00 ^a								
6	4.67 ^b	> 1.00 ^a	1.34 ^b	6.34 ^b	> 1.00 ^a	9.45 ^b	> 1.00 ^a	> 1.00 ^a	5.27 ^c	3.09 ^b	> 1.00 ^a				
7	> 1.00 ^a	1.46 ^b	7.52 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	3.46 ^c	4.01 ^b	> 1.00 ^a					
8	> 1.00 ^a	9.50 ^b	> 1.00 ^a	> 1.00 ^a	2.61 ^b	> 1.00 ^a	> 1.00 ^a	1.04 ^b	8.29 ^b	> 1.00 ^a					
9	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	3.45 ^b	> 1.00 ^a	> 1.00 ^a	2.52 ^b	> 1.00 ^a	> 1.00 ^a	4.75 ^b	> 1.00 ^a	> 1.00 ^a	1.30 ^b	7.14 ^b	> 1.00 ^a
10	5.01 ^c	> 1.00 ^a	2.04 ^b	7.28 ^b	> 1.00 ^a	2.01 ^b	> 1.00 ^a	> 1.00 ^a	1.36 ^b	6.39 ^b	> 1.00 ^a				
11	7.21 ^b	> 1.00 ^a	3.11 ^b	> 1.00 ^a	> 1.00 ^a	2.80 ^b	> 1.00 ^a	> 1.00 ^a	3.12 ^b	> 1.00 ^a	> 1.00 ^a				
HOP-92	1.68 ^b	> 1.00 ^a	1.30 ^b	3.83 ^b	> 1.00 ^a	1.13 ^b	6.12 ^b	> 1.00 ^a	2.09 ^b	6.84 ^b	> 1.00 ^a				
12	> 1.00 ^a	1.47 ^b	6.46 ^b	> 1.00 ^a	1.89 ^b	6.62 ^b	> 1.00 ^a	2.09 ^b	6.87 ^b	> 1.00 ^a					
13	> 1.00 ^a	2.40 ^b	7.54 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	2.44 ^b	> 1.00 ^a	> 1.00 ^a					
14	> 1.00 ^a	4.19 ^b	> 1.00 ^a	> 1.00 ^a	3.31 ^b	> 1.00 ^a	> 1.00 ^a	3.47 ^b	> 1.00 ^a	> 1.00 ^a					
NCI-H460	—	—	—	—	—	—	—	—	—	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	—	—	—
15	4.67 ^b	> 1.00 ^a	1.93 ^b	> 1.00 ^a	1.16 ^b	4.95 ^b	> 1.00 ^a								
16	> 1.00 ^a	1.87 ^b	4.57 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.00 ^a	2.25 ^b	7.20 ^b	> 1.00 ^a					
17	> 1.00 ^a	1.34 ^b	3.64 ^b	9.85 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.97 ^b	8.99 ^b	> 1.00 ^a					
18	> 1.00 ^a	2.45 ^b	> 1.00 ^a	> 1.00 ^a	5.29 ^b	> 1.00 ^a	> 1.00 ^a	2.94 ^b	> 1.00 ^a	> 1.00 ^a					
19	> 1.00 ^a	2.43 ^b	> 1.00 ^a	> 1.00 ^a	2.97 ^b	> 1.00 ^a	> 1.00 ^a	3.06 ^b	> 1.00 ^a	> 1.00 ^a					
20	> 1.00 ^a	3.33 ^b	> 1.00 ^a	> 1.00 ^a	1.00 ^a	> 1.00 ^a	> 1.00 ^a	2.61 ^b	8.31 ^b	> 1.00 ^a					
21	> 1.00 ^a	2.71 ^b	> 1.00 ^a	> 1.00 ^a	1.00 ^a	> 1.00 ^a	> 1.00 ^a	2.69 ^b	> 1.00 ^a	> 1.00 ^a					
22	> 1.00 ^a	3.81 ^b	> 1.00 ^a	> 1.00 ^a	1.00 ^a	> 1.00 ^a	> 1.00 ^a	6.24 ^b	> 1.00 ^a	> 1.00 ^a					
23	> 1.00 ^a	2.81 ^b	> 1.00 ^a	> 1.00 ^a	2.82 ^b	> 1.00 ^a	> 1.00 ^a	2.87 ^b	> 1.00 ^a	> 1.00 ^a					
24	> 1.00 ^a	1.68 ^b	7.37 ^b	> 1.00 ^a	2.19 ^b	> 1.00 ^a	> 1.00 ^a	7.39 ^c	6.58 ^b	> 1.00 ^a					
25	> 1.00 ^a	1.89 ^b	5.25 ^b	> 1.00 ^a	2.39 ^b	> 1.00 ^a	> 1.00 ^a	1.59 ^b	5.51 ^b	> 1.00 ^a					
26	> 1.00 ^a	3.49 ^b	> 1.00 ^a	> 1.00 ^a	2.50 ^b	6.75 ^b	> 1.00 ^a	3.08 ^b	> 1.00 ^a	> 1.00 ^a					
27	1.19 ^b	> 1.00 ^a	4.66 ^c	4.04 ^b	> 1.00 ^a	7.30 ^c	4.00 ^b	> 1.00 ^a	1.91 ^b	7.42 ^b	> 1.00 ^a				
28	> 1.00 ^a	2.89 ^b	> 1.00 ^a	> 1.00 ^a	2.46 ^b	6.03 ^b	> 1.00 ^a	1.65 ^b	4.74 ^b	> 1.00 ^a					
29	> 1.00 ^a	1.90 ^b	9.78 ^b	> 1.00 ^a	8.33 ^b	> 1.00 ^a	> 1.00 ^a	8.02 ^c	3.28 ^b	> 1.00 ^a					
30	> 1.00 ^a	2.28 ^b	9.81 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.98 ^b	> 1.00 ^a	> 1.00 ^a					
31	> 1.00 ^a	2.22 ^b	> 1.00 ^a	> 1.00 ^a	2.39 ^b	> 1.00 ^a	> 1.00 ^a	2.48 ^b	> 1.00 ^a	> 1.00 ^a					
32	> 1.00 ^a	1.82 ^b	5.80 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	2.22 ^b	8.73 ^b	> 1.00 ^a					
33	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
34	7.85 ^b	> 1.00 ^a	1.57 ^b	3.41 ^b	7.44 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.13 ^b	3.28 ^b	9.51 ^b				
35	> 1.00 ^a	1.47 ^b	5.03 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.72 ^b	7.03 ^b	> 1.00 ^a					
36	3.85 ^b	> 1.00 ^a	1.23 ^b	3.47 ^b	9.76 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.25 ^b	4.15 ^b	> 1.00 ^a				
37	7.51 ^b	> 1.00 ^a	1.83 ^b	7.78 ^b	> 1.00 ^a	3.55 ^b	> 1.00 ^a	> 1.00 ^a	1.56 ^b	8.47 ^b	> 1.00 ^a				
38	> 1.00 ^a	1.18 ^b	6.21 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.29 ^b	4.81 ^b	> 1.00 ^a					
3															

43	> 1.00 ^a	4.02 ^b	> 1.00 ^a	> 1.00 ^a	3.32 ^b	> 1.00 ^a	> 1.00 ^a	2.81 ^b	> 1.00 ^a	> 1.00 ^a					
44	> 1.00 ^a	1.75 ^b	6.95 ^b	> 1.00 ^a	2.76 ^b	> 1.00 ^a	> 1.00 ^a	2.83 ^b	7.74 ^b	> 1.00 ^a					
45	> 1.00 ^a	2.03 ^b	9.11 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.42 ^b	> 1.00 ^a	> 1.00 ^a					
46	> 1.00 ^a	2.05 ^b	> 1.00 ^a	1.83 ^b	> 1.00 ^a	> 1.00 ^a									
47	> 1.00 ^a	1.81 ^b	> 1.00 ^a	> 1.00 ^a	1.99 ^b	8.92 ^b	> 1.00 ^a	1.79 ^b	7.05 ^b	> 1.00 ^a					
48	> 1.00 ^a	2.86 ^b	> 1.00 ^a	> 1.00 ^a	3.26 ^b	> 1.00 ^a	> 1.00 ^a	4.70 ^b	> 1.00 ^a	> 1.00 ^a					
49	> 1.00 ^a	2.26 ^b	> 1.00 ^a	> 1.00 ^a	9.67 ^b	> 1.00 ^a	> 1.00 ^a	2.93 ^b	> 1.00 ^a	> 1.00 ^a					
50	8.27 ^b	> 1.00 ^a	1.59 ^b	6.41 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.90 ^b	8.19 ^b	> 1.00 ^a				
51	4.64 ^b	1.00 ^a	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.71 ^b	4.72 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.43 ^b	4.94 ^b	> 1.00 ^a
52	> 1.00 ^a	3.57 ^b	> 1.00 ^a	> 1.00 ^a	3.90 ^b	> 1.00 ^a	> 1.00 ^a	3.52 ^b	> 1.00 ^a	> 1.00 ^a					
53	> 1.00 ^a	3.84 ^b	> 1.00 ^a	> 1.00 ^a	6.51 ^c	> 1.00 ^a	> 1.00 ^a	1.18 ^b	> 1.00 ^a	> 1.00 ^a					
54	> 1.00 ^a	2.33 ^b	6.63 ^b	> 1.00 ^a	6.59 ^b	> 1.00 ^a	> 1.00 ^a	1.12 ^b	5.25 ^b	> 1.00 ^a					
55	> 1.00 ^a	1.94 ^b	> 1.00 ^a	> 1.00 ^a	1.13 ^b	3.63 ^b	> 1.00 ^a	1.60 ^b	6.53 ^b	> 1.00 ^a					
56	3.97 ^b	> 1.00 ^a	2.04 ^b	9.53 ^b	> 1.00 ^a	1.74 ^b	7.12 ^b	> 1.00 ^a	1.59 ^b	6.13 ^b	> 1.00 ^a				
57	> 1.00 ^a	3.12 ^b	9.51 ^b	> 1.00 ^a	1.00 ^a	> 1.00 ^a	> 1.00 ^a	4.54 ^b	> 1.00 ^a	> 1.00 ^a					
58	4.55 ^b	> 1.00 ^a	1.86 ^b	7.66 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	3.61 ^b	> 1.00 ^a	> 1.00 ^a				
59	9.22 ^c	> 1.00 ^a	2.42 ^b	> 1.00 ^a	> 1.00 ^a	2.27 ^b	> 1.00 ^a	> 1.00 ^a	1.87 ^b	> 1.00 ^a	> 1.00 ^a				
60	4.79 ^b	> 1.00 ^a	1.65 ^b	6.63 ^b	> 1.00 ^a	2.93 ^c	> 1.00 ^a	> 1.00 ^a	3.37 ^c	2.91 ^b	> 1.00 ^a				
1	III	IVa	IVb	IVc	IVd										
2	GI ₅₀	TGI	LC ₅₀	GI ₅₀	TGI	LC ₅₀	GI ₅₀	TGI	LC ₅₀	GI ₅₀	TGI	LC ₅₀	GI ₅₀	TGI	LC ₅₀
3	2.67 ^b	8.22 ^b	> 1.00 ^a	1.05 ^b	> 1.00 ^a	> 1.00 ^a	5.55 ^c	> 1.00 ^a	> 1.00 ^a	5.94 ^c	4.68 ^b	> 1.00 ^a	3.53 ^c	2.23 ^b	> 1.00 ^a
4	3.75 ^b	> 1.00 ^a	> 1.00 ^a	—	—	—	5.31 ^c	3.08 ^b	> 1.00 ^a	4.21 ^c	2.21 ^b	> 1.00 ^a	2.91 ^c	> 1.00 ^a	> 1.00 ^a
5	3.10 ^b	> 1.00 ^a	> 1.00 ^a	8.38 ^c	> 1.00 ^a	> 1.00 ^a	8.61 ^c	> 1.00 ^a	> 1.00 ^a	1.37 ^b	> 1.00 ^a	> 1.00 ^a	1.06 ^b	> 1.00 ^a	> 1.00 ^a
6	9.20 ^b	> 1.00 ^a	> 1.00 ^a	2.29 ^b	> 1.00 ^a	> 1.00 ^a	2.31 ^b	> 1.00 ^a	> 1.00 ^a	2.32 ^b	9.01 ^c	> 1.00 ^a	1.09 ^b	7.97 ^b	> 1.00 ^a
7	4.67 ^b	> 1.00 ^a	> 1.00 ^a	—	—	—	—	—	—	—	—	—	—	—	—
8	3.00 ^b	> 1.00 ^a	> 1.00 ^a	—	—	—	—	—	—	—	—	—	—	—	—
9	> 1.00 ^a	7.18 ^b	> 1.00 ^a	> 1.00 ^a	9.61 ^b	> 1.00 ^a	> 1.00 ^a	2.46 ^b	6.68 ^b	> 1.00 ^a					
10	9.21 ^b	> 1.00 ^a	> 1.00 ^a	2.58 ^b	7.93 ^b	> 1.00 ^a	2.75 ^b	7.77 ^b	> 1.00 ^a	2.86 ^b	9.10 ^b	> 1.00 ^a	1.85 ^b	4.88 ^b	> 1.00 ^a
11	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	—	—	—	—	—	—	—	—	—	—	—	—
HOP-92	—	—	—	1.38 ^b	2.92 ^b	6.16 ^b	1.65 ^b	3.51 ^b	7.47 ^b	1.38 ^b	2.93 ^b	6.20 ^b	5.06 ^c	1.85 ^b	4.87 ^b
12	> 1.00 ^a	9.87 ^b	> 1.00 ^a	2.29 ^b	7.12 ^b	> 1.00 ^a									
13	4.60 ^b	> 1.00 ^a	> 1.00 ^a	2.61 ^b	7.05 ^b	> 1.00 ^a	2.61 ^b	8.58 ^b	> 1.00 ^a	2.10 ^b	5.27 ^b	> 1.00 ^a	1.67 ^b	3.72 ^b	8.28 ^b
14	> 1.00 ^a	8.58 ^b	> 1.00 ^a	> 1.00 ^a	6.97 ^b	> 1.00 ^a	> 1.00 ^a	2.54 ^b	7.65 ^b	> 1.00 ^a					
NCI-H460	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	2.57 ^b	> 1.00 ^a	> 1.00 ^a	4.74 ^c	3.21 ^b	> 1.00 ^a	1.97 ^b	> 1.00 ^a	> 1.00 ^a	1.59 ^b	2.94 ^b	5.42 ^b
15	1.93 ^b	4.78 ^b	> 1.00 ^a	—	—	—	—	—	—	—	—	—	—	—	—
16	7.54 ^b	> 1.00 ^a	> 1.00 ^a	1.18 ^b	3.15 ^b	8.40 ^b	1.46 ^b	3.35 ^b	7.66 ^b	1.47 ^b	3.85 ^b	> 1.00 ^a	6.40 ^c	1.92 ^b	4.38 ^b
17	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.51 ^b	3.10 ^b	6.39 ^b	1.34 ^b	2.96 ^b	6.54 ^b	2.55 ^b	5.01 ^b	9.85 ^b	—	—	—
18	6.31 ^b	> 1.00 ^a	> 1.00 ^a	1.74 ^b	3.85 ^b	8.25 ^b	1.60 ^b	3.98 ^b	9.89 ^b	1.66 ^b	3.62 ^b	7.92 ^b	1.25 ^b	2.51 ^b	5.01 ^b
19	9.29 ^b	> 1.00 ^a	> 1.00 ^a	9.23 ^c	2.55 ^b	5.16 ^b	9.47 ^c	2.35 ^b	5.66 ^b	1.53 ^b	3.76 ^b	9.24 ^b	—	—	—
20	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	2.68 ^b	> 1.00 ^a	> 1.00 ^a	1.45 ^b	4.38 ^b	> 1.00 ^a	2.71 ^b	> 1.00 ^a	> 1.00 ^a	1.13 ^b	2.61 ^b	6.03 ^b
21	6.45 ^b	> 1.00 ^a	> 1.00 ^a	3.38 ^b	> 1.00 ^a	> 1.00 ^a	—	—	—	2.42 ^b	6.11 ^b	> 1.00 ^a	—	—	—
22	5.09 ^b	> 1.00 ^a	> 1.00 ^a	7.76 ^c	5.23 ^b	> 1.00 ^a	1.37 ^b	9.93 ^b	> 1.00 ^a	8.75 ^c	9.83 ^b	> 1.00 ^a	1.03 ^b	> 1.00 ^a	> 1.00 ^a
23	9.75 ^b	> 1.00 ^a	> 1.00 ^a	3.08 ^b	6.74 ^b	> 1.00 ^a	1.92 ^b	4.66 ^b	> 1.00 ^a	2.47 ^b	6.03 ^b	> 1.00 ^a	1.27 ^b	2.53 ^b	5.03 ^b
24	> 1.00 ^a	4.99 ^b	> 1.00 ^a	> 1.00 ^a	7.00 ^b	> 1.00 ^a	> 1.00 ^a	1.95 ^b	4.13 ^b	9.25 ^b					
25	9.37 ^b	> 1.00 ^a	> 1.00 ^a	2.38 ^b	5.16 ^b	> 1.00 ^a	1.80 ^b	3.94 ^b	8.62 ^b	2.18 ^b	4.15 ^b	9.31 ^b	1.39 ^b	2.75 ^b	5.45 ^b
26	8.74 ^b	> 1.00 ^a	> 1.00 ^a	3.16 ^b	> 1.00 ^a	> 1.00 ^a	3.42 ^b	> 1.00 ^a	> 1.00 ^a	2.28 ^b	6.52 ^b	> 1.00 ^a	1.78 ^b	3.60 ^b	7.28 ^b
27	—	—	—	5.55 ^b	> 1.00 ^a	> 1.00 ^a	2.84 ^b	> 1.00 ^a	> 1.00 ^a	3.82 ^b	> 1.00 ^a	> 1.00 ^a	1.40 ^b	3.52 ^b	8.87 ^b
28	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	—	—	—	1.74 ^b	6.39 ^b	> 1.00 ^a	2.28 ^b	7.15 ^b	> 1.00 ^a	8.88 ^c	4.55 ^b	> 1.00 ^a
29	4.46 ^b	> 1.00 ^a	> 1.00 ^a	1.72 ^b	3.75 ^b	8.17<									

30	9.08 ^b	> 1.00 ^a	> 1.00 ^a	2.37 ^b	4.38 ^b	9.85 ^b	1.68 ^b	3.96 ^b	9.13 ^b	2.04 ^b	4.35 ^b	9.30 ^b	1.63 ^b	3.56 ^b	7.78 ^b	
31	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	2.04 ^b	4.16 ^b	8.46 ^b	1.28 ^b	2.98 ^b	6.93 ^b	2.01 ^b	4.03 ^b	8.08 ^b	1.06 ^b	2.24 ^b	4.74 ^b	
32	2.99 ^b	> 1.00 ^a	> 1.00 ^a	1.76 ^b	4.53 ^b	> 1.00 ^a	2.60 ^b	7.60 ^b	> 1.00 ^a	1.99 ^b	4.35 ^b	9.53 ^b	1.27 ^b	2.53 ^b	5.03 ^b	
33	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.56 ^b	4.56 ^b	> 1.00 ^a	2.74 ^b	8.73 ^b	> 1.00 ^a	2.17 ^b	5.60 ^b	> 1.00 ^a	1.45 ^b	4.68 ^b	> 1.00 ^a	
34	3.86 ^b	> 1.00 ^a	> 1.00 ^a	1.55 ^b	3.13 ^b	6.32 ^b	1.68 ^b	3.57 ^b	7.59 ^b	1.63 ^b	3.23 ^b	6.41 ^b	1.14 ^b	2.35 ^b	4.84 ^b	
35	6.55 ^b	> 1.00 ^a	> 1.00 ^a	1.77 ^b	3.49 ^b	6.86 ^b	2.06 ^b	4.95 ^b	> 1.00 ^a	1.80 ^b	3.76 ^b	7.82 ^b	1.74 ^b	3.41 ^b	6.69 ^b	
36	3.29 ^b	> 1.00 ^a	> 1.00 ^a	1.66 ^b	3.64 ^b	7.95 ^b	2.06 ^b	5.80 ^b	> 1.00 ^a	—	—	—	1.47 ^b	3.39 ^b	7.82 ^b	
37	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.83 ^b	4.03 ^b	8.88 ^b	—	—	—	1.96 ^b	4.19 ^b	8.96 ^b	1.46 ^b	2.77 ^b	5.26	
38	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.61 ^b	3.35 ^b	6.95 ^b	2.27 ^b	5.98 ^b	> 1.00 ^a	1.77 ^b	3.65 ^b	7.54 ^b	1.11 ^b	2.31 ^b	4.81 ^b	
39	1.84 ^b	> 1.00 ^a	> 1.00 ^a	—	—	—	—	—	—	—	—	—	—	—	—	
40	8.75 ^b	> 1.00 ^a	> 1.00 ^a	2.49 ^b	6.18 ^b	> 1.00 ^a	2.01 ^b	4.75 ^b	> 1.00 ^a	2.20 ^b	5.26 ^b	> 1.00 ^a	1.66 ^b	3.04 ^b	5.56 ^b	
41	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	2.32 ^b	7.36 ^b	> 1.00 ^a	2.02 ^b	4.98 ^b	> 1.00 ^a	2.07 ^b	5.41 ^b	> 1.00 ^a	—	—	—	
42	8.04 ^b	> 1.00 ^a	4.57 ^b	> 1.00 ^a	> 1.00 ^a											
43	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.44 ^b	3.12 ^b	6.72 ^b	1.42 ^b	3.44 ^b	8.37 ^b	1.28 ^b	2.86 ^b	6.37 ^b	1.93 ^b	> 1.00 ^a	> 1.00 ^a	
44	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	2.19 ^b	5.77 ^b	> 1.00 ^a	2.53 ^b	6.00 ^b	> 1.00 ^a	2.72 ^b	6.16 ^b	> 1.00 ^a	1.83 ^b	3.93 ^b	8.47 ^b	
45	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	2.85 ^a	9.42 ^a	> 1.00 ^a	3.31 ^b	> 1.00 ^a	> 1.00 ^a	1.99 ^b	4.28 ^b	9.23 ^b	1.51 ^b	3.01 ^b	6.00 ^b	
46	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.16 ^b	2.45 ^b	5.16 ^b	8.33 ^c	2.24 ^b	5.43 ^b	6.91 ^c	1.98 ^b	4.71 ^b	3.59 ^c	1.42 ^b	3.77 ^b	
47	3.45 ^b	> 1.00 ^a	> 1.00 ^a	2.17 ^b	5.91 ^b	> 1.00 ^a	2.05 ^b	4.64 ^b	> 1.00 ^a	1.97 ^b	4.45 ^b	> 1.00 ^a	1.31 ^b	2.58 ^b	5.09 ^b	
48	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.48 ^b	2.92 ^b	5.78 ^b	1.52 ^b	3.14 ^b	6.49 ^b	1.53 ^b	3.01 ^b	5.93 ^b	1.23 ^b	2.48 ^b	4.98 ^b	
49	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.72 ^b	3.61 ^b	7.58 ^b	1.99 ^b	4.84 ^b	> 1.00 ^a	2.25 ^b	4.68 ^b	9.73 ^b	1.62 ^b	3.16 ^b	6.15 ^b	
50	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	3.04 ^b	> 1.00 ^a	> 1.00 ^a	3.28 ^b	> 1.00 ^a	> 1.00 ^a	—	—	—	1.52 ^b	3.06 ^b	6.14 ^b	
51	4.60 ^b	> 1.00 ^a	> 1.00 ^a	2.29 ^b	6.46 ^b	> 1.00 ^a	3.04 ^b	> 1.00 ^a	> 1.00 ^a	2.44 ^b	6.92 ^b	> 1.00 ^a	1.38 ^b	2.73 ^b	5.38 ^b	
52	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	2.59 ^b	9.00 ^b	> 1.00 ^a	2.63 ^b	9.48 ^b	> 1.00 ^a	2.43 ^b	6.65 ^b	> 1.00 ^a	1.53 ^b	2.87 ^b	5.35 ^b	
53	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	2.19 ^b	5.40 ^b	> 1.00 ^a	1.21 ^b	3.65 ^b	> 1.00 ^a	2.08 ^b	5.23 ^b	> 1.00 ^a	1.17 ^b	2.95 ^b	7.44 ^b	
54	> 1.00 ^a	1.00 ^a	> 1.00 ^a	4.42 ^b	> 1.00 ^a	> 1.00 ^a	3.49 ^b	> 1.00 ^a	> 1.00 ^a	3.74 ^b	> 1.00 ^a	> 1.00 ^a	2.82 ^b	> 1.00 ^a	> 1.00 ^a	
55	6.46 ^b	> 1.00 ^a	> 1.00 ^a	1.67 ^b	3.30 ^b	6.53 ^b	1.96 ^b	3.97 ^b	8.05 ^b	1.57 ^b	3.21 ^b	6.57 ^b	1.52 ^b	3.33 ^b	7.27 ^b	
56	4.75 ^b	> 1.00 ^a	> 1.00 ^a	3.07 ^b	7.04 ^b	> 1.00 ^a	1.64 ^b	4.23 ^b	> 1.00 ^a	2.18 ^b	5.78 ^b	> 1.00 ^a	1.71 ^b	4.47 ^b	> 1.00 ^a	
57	4.05 ^b	> 1.00 ^a	> 1.00 ^a	1.98 ^b	5.28 ^b	> 1.00 ^a	2.36 ^b	8.06 ^b	> 1.00 ^a	2.08 ^b	5.09 ^b	> 1.00 ^a	1.89 ^b	6.47 ^b	> 1.00 ^a	
58	4.92 ^b	> 1.00 ^a	> 1.00 ^a	1.74 ^b	3.38 ^b	6.57 ^b	1.58 ^b	3.27 ^b	6.76 ^b	1.84 ^b	3.58 ^b	6.97 ^b	1.29 ^b	2.55 ^b	5.05 ^b	
59	1.99 ^b	7.35	> 1.00 ^a	1.56 ^b	3.03 ^b	5.91 ^b	1.88 ^b	3.98 ^b	8.42 ^b	1.77 ^b	3.44 ^b	6.70 ^b	1.54 ^b	3.05 ^b	6.04 ^b	
60	—	—	—	1.76 ^b	5.18 ^b	> 1.00 ^a	1.76 ^b	7.17 ^b	> 1.00 ^a	1.88 ^b	5.36 ^b	> 1.00 ^a	1.10 ^b	2.67 ^b	6.52 ^b	
1	IVe				IVf				IVg				IVi		IVj	
2	GI ₅₀	TGI	LC ₅₀													
3	1.56 ^b	5.22 ^b	> 1.00 ^a	1.76 ^b	6.76 ^b	> 1.00 ^a	2.35 ^b	8.44 ^b	> 1.00 ^a	1.60 ^b	5.14	> 1.00 ^a	1.60 ^b	5.13 ^b	> 1.00 ^a	
4	1.38 ^b	3.90 ^b	> 1.00 ^a	1.66 ^b	4.01 ^b	9.69 ^b	1.88 ^b	4.83 ^b	> 1.00 ^a	1.59 ^b	3.70 ^b	8.61 ^b	1.41 ^b	4.11 ^b	> 1.00 ^a	
5	1.46 ^b	> 1.00 ^a	> 1.00 ^a	2.51 ^b	> 1.00 ^a	> 1.00 ^a	3.49 ^b	> 1.00 ^a	> 1.00 ^a	3.00 ^b	> 1.00 ^a	> 1.00 ^a	3.49 ^b	> 1.00 ^a	> 1.00 ^a	
6	3.63 ^b	> 1.00 ^a	> 1.00 ^a	2.54 ^b	> 1.00 ^a	> 1.00 ^a	3.22 ^b	> 1.00 ^a	> 1.00 ^a	3.01 ^b	> 1.00 ^a	> 1.00 ^a	3.60 ^b	> 1.00 ^a	> 1.00 ^a	
7	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	
8	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	
9	> 1.00 ^a	7.91 ^b	> 1.00 ^a	> 1.00 ^a												
10	2.79 ^b	9.83 ^b	> 1.00 ^a	2.14 ^b	5.66 ^b	> 1.00 ^a	3.40 ^b	> 1.00 ^a	> 1.00 ^a	1.87 ^b	5.34 ^b	> 1.00 ^a	3.08 ^b	> 1.00 ^a	> 1.00 ^a	
11	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	
HOP-92	1.35 ^b	3.31 ^b	8.07 ^b	1.26 ^b	2.97 ^b	6.98 ^b	2.23 ^b	4.73 ^b	> 1.00 ^a	1.78 ^b	3.47 ^b	6.77 ^{bb}	1.69 ^b	3.76 ^b	8.35 ^b	
12	> 1.00 ^a															
13	3.36 ^b	> 1.00 ^a	> 1.00 ^a	2.83 ^b	7.82 ^b	> 1.00 ^a	2.99 ^b	9.36 ^b	> 1.00 ^a	3.07 ^b	> 1.00 ^a	> 1.00 ^a	2.88 ^b	8.68 ^b	> 1.00 ^a	
14	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	7.22 ^b	> 1.00 ^a	> 1.00 ^a	5.01 ^b	1.93 ^b	> 1.00 ^a	4.46 ^b	> 1.00 ^a	1.59 ^b	3.38 ^b	7.22 ^b	1.96 ^b	
NCI-H460	1.35 ^b	2.97 ^b	6.51 ^b	1.26 ^b	2.51 ^b	5.01 ^b	1.36 ^b	2.77 ^b	5.62 ^b	1.45 ^b	2.76 ^b	5.26 ^b	1.21 ^b	2.45 ^b	4.95 ^b	
15	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	
16	1.38 ^b	2.75 ^b	5.46 ^b	1.64 ^b	3.04 ^b	5.64 ^b	1.36 ^b	2.77 ^b	5.62 ^b	1.45 ^b	2.76 ^b	5.26 ^b	1.21 ^b	2.45 ^b	4.95 ^b	

	IVk				IVm				IVn			
2	GI ₅₀	TGI	LC ₅₀									
3	2.27 ^b	> 1.00 ^a	> 1.00 ^a	2.69 ^b	6.91 ^b	> 1.00 ^a	5.24 ^b	> 1.00 ^a	> 1.00 ^a			
4	1.55 ^b	3.82 ^b	9.39 ^b	4.42 ^b	> 1.00 ^a	> 1.00 ^a	—	—	—			
17	—	—	—	1.08 ^b	2.27 ^b	4.77 ^b	2.68 ^b	5.55 ^b	> 1.00 ^a	1.37 ^b	3.07 ^b	6.90 ^b
18	1.85 ^b	4.04 ^b	8.83 ^b	2.12 ^b	4.98 ^b	> 1.00 ^a	2.67 ^b	6.71 ^b	> 1.00 ^a	2.71 ^b	7.82 ^b	> 1.00 ^a
19	—	—	—	1.09 ^b	2.29 ^b	4.78 ^b	1.25 ^b	2.50 ^b	5.00 ^b	1.28 ^b	2.53 ^b	5.03 ^b
20	2.63 ^b	7.46 ^b	> 1.00 ^a	1.81 ^b	4.58 ^b	> 1.00 ^a	3.28 ^b	> 1.00 ^a	> 1.00 ^a	1.63 ^b	4.10 ^b	> 1.00 ^a
21	4.49 ^b	> 1.00 ^a	> 1.00 ^a	5.15 ^b	> 1.00 ^a	> 1.00 ^a	5.98 ^b	> 1.00 ^a	> 1.00 ^a	5.20 ^b	> 1.00 ^a	> 1.00 ^a
22	1.27 ^b	3.13 ^b	7.71 ^b	—	—	—	1.64 ^b	4.04 ^b	9.94 ^b	2.66 ^b	8.05 ^b	> 1.00 ^a
23	3.29 ^b	> 1.00 ^a	> 1.00 ^a	2.55 ^b	7.60 ^b	> 1.00 ^a	2.90 ^b	> 1.00 ^a	> 1.00 ^a	2.01 ^b	5.63 ^b	> 1.00 ^a
24	8.48 ^b	> 1.00 ^a	> 1.00 ^a	8.65 ^b	> 1.00 ^a	9.01 ^b	> 1.00 ^a					
25	1.89 ^b	3.42 ^b	6.18 ^b	2.03 ^b	4.03 ^b	7.99 ^b	1.94 ^b	3.59 ^b	6.63 ^b	2.46 ^b	6.60 ^b	> 1.00 ^a
26	3.71 ^b	> 1.00 ^a	> 1.00 ^a	5.51 ^b	> 1.00 ^a	> 1.00 ^a	4.24 ^b	> 1.00 ^a	> 1.00 ^a	—	—	—
27	4.06 ^b	> 1.00 ^a	9.73 ^b	> 1.00 ^a	> 1.00 ^a	3.21 ^b	> 1.00 ^a	> 1.00 ^a				
28	2.19 ^b	5.38 ^b	> 1.00 ^a	1.87 ^b	4.66 ^b	> 1.00 ^a	2.44 ^b	5.15 ^b	> 1.00 ^a	2.42 ^b	6.57 ^b	> 1.00 ^a
29	1.69 ^b	3.59 ^b	7.65 ^b	1.72 ^b	3.69 ^b	7.92 ^b	1.92 ^b	4.05 ^b	8.52 ^b	1.90 ^b	4.15 ^b	9.08 ^b
30	2.62 ^b	7.30 ^b	> 1.00 ^a	2.83 ^b	9.03 ^b	> 1.00 ^a	3.12 ^b	8.87 ^b	> 1.00 ^a	1.96 ^b	5.78 ^b	> 1.00 ^a
31	1.91 ^b	3.87 ^b	7.86 ^b	1.39 ^b	2.80 ^b	5.61 ^b	1.91 ^b	3.59 ^b	6.75 ^b	1.45 ^b	3.05 ^b	6.38 ^b
32	1.99 ^b	6.17 ^b	> 1.00 ^a	1.69 ^b	4.27 ^b	> 1.00 ^a	2.94 ^b	7.59 ^b	> 1.00 ^a	1.76 ^b	6.77 ^b	> 1.00 ^a
33	1.76 ^b	4.75 ^b	> 1.00 ^a	—	—	—	1.84 ^b	4.62 ^b	> 1.00 ^a	3.71 ^b	> 1.00 ^a	> 1.00 ^a
34	8.00 ^c	2.09 ^b	4.57 ^b	1.67 ^b	3.03 ^b	5.51 ^b	1.49 ^b	2.81 ^b	5.30 ^b	1.38 ^b	2.66 ^b	5.16 ^b
35	1.96 ^b	4.96 ^b	> 1.00 ^a	2.53 ^b	6.87 ^b	> 1.00 ^a	2.05 ^b	5.19 ^b	> 1.00 ^a	2.85 ^b	> 1.00 ^a	> 1.00 ^a
36	1.79 ^b	4.27 ^b	> 1.00 ^a	2.44 ^b	5.64 ^b	> 1.00 ^a	1.77 ^b	3.68 ^b	7.65 ^b	2.76 ^b	8.05 ^b	> 1.00 ^a
37	4.26 ^b	> 1.00 ^a	> 1.00 ^a	3.38 ^b	> 1.00 ^a	> 1.00 ^a	5.89 ^b	> 1.00 ^a	> 1.00 ^a	—	—	—
38	—	—	—	1.51 ^b	2.91 ^b	5.59 ^b	2.13 ^b	4.79 ^b	> 1.00 ^a	1.77 ^b	3.34 ^b	6.29 ^b
39	—	—	—	—	—	—	—	—	—	—	—	—
40	3.47 ^b	> 1.00 ^a	> 1.00 ^a	2.55 ^b	6.95 ^b	> 1.00 ^a	2.97 ^b	8.36 ^b	> 1.00 ^a	2.56 ^b	7.11 ^b	> 1.00 ^a
41	2.96 ^b	> 1.00 ^a	> 1.00 ^a	3.04 ^b	> 1.00 ^a	> 1.00 ^a	3.99 ^b	> 1.00 ^a	> 1.00 ^a	2.58 ^b	7.95 ^b	> 1.00 ^a
42	> 1.00 ^a											
43	1.74 ^b	4.52 ^b	> 1.00 ^a	2.12 ^b	5.11 ^b	> 1.00 ^a	2.08 ^b	4.95 ^b	> 1.00 ^a	1.49 ^b	5.17 ^b	> 1.00 ^a
44	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	4.21 ^b	> 1.00 ^a	6.74 ^b	> 1.00 ^a	> 1.00 ^a				
45	3.40 ^b	> 1.00 ^a	> 1.00 ^a	3.81 ^b	> 1.00 ^a	> 1.00 ^a	3.66 ^b	> 1.00 ^a	> 1.00 ^a	3.60 ^b	> 1.00 ^a	3.33 ^b
46	1.21 ^b	2.44 ^b	4.95 ^b	1.37 ^b	2.66 ^b	5.16 ^b	1.44 ^b	2.74 ^b	5.24 ^b	1.09 ^b	2.28 ^b	4.78 ^b
47	2.14 ^b	4.39 ^b	9.02 ^b	3.03 ^b	8.75 ^b	> 1.00 ^a	2.26 ^b	5.14 ^b	> 1.00 ^a	3.62 ^b	> 1.00 ^a	1.82 ^b
48	1.49 ^b	2.81 ^b	5.30 ^b	1.66 ^b	3.20 ^b	6.18 ^b	1.67 ^b	3.04 ^b	5.52 ^b	1.39 ^b	2.68 ^b	5.18 ^b
49	4.20 ^b	> 1.00 ^a	> 1.00 ^a	3.59 ^b	> 1.00 ^a	> 1.00 ^a	3.79 ^b	> 1.00 ^a	> 1.00 ^a	4.71 ^b	> 1.00 ^a	> 1.00 ^a
50	3.55 ^b	> 1.00 ^a	> 1.00 ^a	3.98 ^b	> 1.00 ^a	> 1.00 ^a	3.86 ^b	> 1.00 ^a	> 1.00 ^a	4.57 ^b	> 1.00 ^a	4.29 ^b
51	3.09 ^b	> 1.00 ^a	> 1.00 ^a	2.27 ^b	8.87 ^b	> 1.00 ^a	3.66 ^b	> 1.00 ^a	> 1.00 ^a	2.46 ^b	> 1.00 ^a	3.19 ^b
52	2.84 ^b	> 1.00 ^a	> 1.00 ^a	3.13 ^b	> 1.00 ^a	> 1.00 ^a	3.10 ^b	> 1.00 ^a	> 1.00 ^a	2.84 ^b	> 1.00 ^a	2.57 ^b
53	2.29 ^b	5.02 ^b	> 1.00 ^a	2.12 ^b	4.93 ^b	> 1.00 ^a	2.24 ^b	5.15 ^b	> 1.00 ^a	1.87 ^b	4.17 ^b	9.30 ^b
54	6.49 ^b	> 1.00 ^a	> 1.00 ^a	4.29	> 1.00 ^a	5.49 ^b	> 1.00 ^a	7.71 ^b				
55	1.46 ^b	3.20 ^b	7.03 ^b	1.69 ^b	3.54 ^b	7.40 ^b	1.90 ^b	3.95 ^b	8.18 ^b	1.54 ^b	3.18 ^b	6.57 ^b
56	2.71 ^b	> 1.00 ^a	> 1.00 ^a	2.46 ^b	7.86 ^b	> 1.00 ^a	2.49 ^b	8.08 ^b	> 1.00 ^a	2.43 ^b	6.94 ^b	> 1.00 ^a
57	—	> 1.00 ^a	> 1.00 ^a	3.33 ^b	> 1.00 ^a	> 1.00 ^a	—	6.39 ^b	> 1.00 ^a	3.78 ^b	> 1.00 ^a	> 1.00 ^a
58	1.65 ^b	3.24 ^b	6.35 ^b	1.82 ^b	4.44 ^b	> 1.00 ^a	1.98 ^b	4.30 ^b	9.35 ^b	1.52 ^b	2.98 ^b	5.83 ^b
59	3.10 ^b	> 1.00 ^a	> 1.00 ^a	4.23 ^b	> 1.00 ^a	> 1.00 ^a	3.25 ^b	> 1.00 ^a	> 1.00 ^a	5.17 ^b	> 1.00 ^a	3.16 ^b
60	1.37 ^b	3.59 ^b	9.41 ^b	2.00 ^b	5.53 ^b	> 1.00 ^a	1.78 ^b	4.59 ^b	> 1.00 ^a	1.50 ^b	3.35 ^b	7.47 ^b
1	IVk				IVm				IVn			
2	GI ₅₀	TGI	LC ₅₀									
3	2.27 ^b	> 1.00 ^a	> 1.00 ^a	2.69 ^b	6.91 ^b	> 1.00 ^a	5.24 ^b	> 1.00 ^a	> 1.00 ^a			
4	1.55 ^b	3.82 ^b	9.39 ^b	4.42 ^b	> 1.00 ^a	> 1.00 ^a	—	—	—			

5	3.28 ^b	> 1.00 ^a	> 1.00 ^a	7.56 ^b	> 1.00 ^a	> 1.00 ^a	7.11 ^b	> 1.00 ^a	> 1.00 ^a
6	2.73 ^b	> 1.00 ^a	> 1.00 ^a	5.43 ^b	> 1.00 ^a	> 1.00 ^a	2.15 ^b	> 1.00 ^a	> 1.00 ^a
7	—	—	—	—	—	—	—	—	—
8	—	—	—	—	—	—	—	—	—
9	> 1.00 ^a								
10	1.92 ^b	5.27 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	2.35 ^b	6.06 ^b	> 1.00 ^a
11	—	—	—	—	—	—	—	—	—
HOP-92	2.19 ^b	4.89 ^b	> 1.00 ^a	5.27 ^b	> 1.00 ^a	> 1.00 ^a	1.55 ^b	3.36 ^b	7.30 ^b
12	6.71 ^b	> 1.00 ^a							
13	2.93 ^b	8.69 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	3.05 ^b	> 1.00 ^a	> 1.00 ^a
14	> 1.00 ^a	6.20 ^b	> 1.00 ^a	> 1.00 ^a					
NCI-H460	1.86 ^b	4.22 ^b	9.60 ^b	6.37 ^b	> 1.00 ^a	> 1.00 ^a	1.90 ^b	4.97 ^b	> 1.00 ^a
15	—	—	—	—	—	—	—	—	—
16	1.47 ^b	2.78 ^b	5.27 ^b	3.78 ^b	> 1.00 ^a	> 1.00 ^a	1.34 ^b	3.41 ^b	8.66 ^b
17	—	—	—	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.42 ^b	2.90 ^b	5.95 ^b
18	1.83 ^b	4.21 ^b	9.65 ^b	6.42 ^b	> 1.00 ^a	> 1.00 ^a	1.70 ^b	4.14 ^b	> 1.00 ^a
19	1.35 ^b	2.63 ^b	5.13 ^b	4.07 ^b	> 1.00 ^a	> 1.00 ^a	1.24 ^b	2.86 ^b	6.60 ^b
20	1.50 ^b	3.53 ^b	7.89 ^b	6.92 ^b	> 1.00 ^a	> 1.00 ^a	1.82 ^b	6.02 ^b	> 1.00 ^a
21	3.62 ^b	> 1.00 ^a	8.49 ^c	2.58 ^b	6.96 ^b				
22	2.59 ^b	> 1.00 ^a	> 1.00 ^a	5.36 ^b	> 1.00 ^a	> 1.00 ^a	1.48 ^b	> 1.00 ^a	> 1.00 ^a
23	2.27 ^b	7.43 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	2.49 ^c	1.81 ^b	4.96 ^b
24	7.81 ^b	> 1.00 ^a	6.90 ^b	> 1.00 ^a	> 1.00 ^a				
25	2.31 ^b	5.73 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.71 ^b	4.21 ^b	> 1.00 ^a
26	4.35 ^b	> 1.00 ^a	4.60 ^b	> 1.00 ^a	> 1.00 ^a				
27	9.68 ^b	> 1.00 ^a	2.13 ^b	1.17 ^b	> 1.00 ^a				
28	1.63 ^b	4.04 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.76 ^b	6.96 ^b	> 1.00 ^a
29	1.77 ^b	4.04 ^b	9.19 ^b	4.93 ^b	> 1.00 ^a	> 1.00 ^a	1.73 ^b	4.51 ^b	> 1.00 ^a
30	1.84 ^b	5.18 ^b	> 1.00 ^a	2.42 ^b	9.08 ^b	> 1.00 ^a	1.70 ^b	3.45 ^b	7.00 ^b
31	1.62 ^b	3.92 ^b	9.15 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.27 ^b	2.87 ^b	6.48 ^b
32	1.44 ^b	3.35 ^b	7.80 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	2.02 ^b	4.30 ^b	9.15 ^b
33	2.48 ^b	9.76 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	—	—	—
34	1.13 ^b	2.34 ^b	4.84 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.61 ^b	3.30 ^b	6.75 ^b
35	2.39 ^b	7.12	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.80 ^b	3.73 ^b	7.72 ^b
36	2.49 ^b	7.61 ^b	> 1.00 ^a	2.49 ^b	> 1.00 ^a	> 1.00 ^a	1.79 ^b	4.94 ^b	> 1.00 ^a
37	3.30 ^b	> 1.00 ^a	1.90 ^b	3.72 ^b	7.29 ^b				
38	1.51 ^b	2.84 ^b	5.33 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.36 ^b	2.82 ^b	5.85 ^b
39	—	—	—	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	—	—	—
40	2.91 ^b	8.56 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	2.12 ^b	5.06 ^b	> 1.00 ^a
41	2.39 ^b	8.42 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	2.10 ^b	4.89 ^b	> 1.00 ^a
42	> 1.00 ^a								
43	2.13 ^b	5.53 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.46 ^b	3.37 ^b	7.78 ^b
44	8.87 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	> 1.00 ^b	> 1.00 ^a	1.78 ^b	4.89 ^b	> 1.00 ^a
45	3.65 ^b	> 1.00 ^a	3.61 ^b	> 1.00 ^a	> 1.00 ^a				
46	1.25 ^b	2.50 ^b	5.00 ^b	3.19 ^b	> 1.00 ^a	> 1.00 ^a	1.08 ^b	2.45 ^b	5.56 ^b
47	2.73 ^b	6.57 ^b	> 1.00 ^a	5.98 ^b	> 1.00 ^a	> 1.00 ^a	3.19 ^b	> 1.00 ^a	> 1.00 ^a
48	1.57 ^b	2.91 ^b	5.40 ^b	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.31 ^b	2.67 ^b	5.41 ^b
49	3.70 ^b	> 1.00 ^a	1.66 ^b	3.76 ^b	8.52 ^b				
50	3.62 ^b	> 1.00 ^a	3.49 ^b	> 1.00 ^a	> 1.00 ^a				

38	> 1.00 ^a	—	—	—						
39	> 1.00 ^a									
40	> 1.00 ^a									
41	> 1.00 ^a									
42	> 1.00 ^a									
43	> 1.00 ^a									
44	> 1.00 ^a									
45	> 1.00 ^a									
46	> 1.00 ^a									
47	> 1.00 ^a									
48	> 1.00 ^a									
49	> 1.00 ^a									
50	> 1.00 ^a									
51	> 1.00 ^a									
52	> 1.00 ^a									
53	> 1.00 ^a	7.50 ^b	> 1.00 ^a	> 1.00 ^a						
54	> 1.00 ^a									
55	> 1.00 ^a									
56	> 1.00 ^a									
57	> 1.00 ^a									
58	> 1.00 ^a									
59	> 1.00 ^a									
60	> 1.00 ^a									
1	VIIb					VIIa				
2	GI ₅₀	TGI	LC ₅₀	GI ₅₀	TGI	LC ₅₀				
3	2.30 ^b	9.19 ^b	> 1.00 ^a	3.34 ^d	2.37 ^c	> 1.00 ^a				
4	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	2.86 ^d	8.84 ^d	—				
5	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	2.42 ^c	1.31 ^d	> 1.00 ^a				
6	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	4.74 ^d	—	> 1.00 ^a				
7	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	—	—	—				
8	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.91 ^c	5.56 ^c	3.89 ^b				
9	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.86 ^b	3.26 ^b	5.71 ^b				
10	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.04 ^b	2.22 ^b	4.71 ^b				
11	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.94 ^b	4.25 ^b	9.30 ^b				
HOP-92	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	5.36 ^c	1.96 ^b	5.49 ^b				
12	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	2.08 ^b	4.07 ^b	7.95 ^b				
13	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.32 ^b	3.03 ^b	6.91 ^b				
14	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.84 ^b	3.35 ^b	6.10 ^b				
NC ₁ -H460	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	2.57 ^b	7.93 ^b	> 1.00 ^a				
15	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	5.73 ^d	2.97 ^c	1.97 ^b				
16	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.31 ^c	2.64 ^c	5.33 ^c				
17	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	2.41 ^b	6.70 ^b	> 1.00 ^a				
18	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.56 ^c	2.90 ^c	5.39 ^b				
19	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	3.06 ^c	1.47 ^b	> 1.00 ^a				
20	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	2.28 ^c	6.92 ^c	2.52 ^b				
21	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.41 ^b	2.71 ^b	5.20 ^b				
22	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.17 ^c	2.46 ^c	5.14 ^c				
23	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.32 ^b	3.22 ^b	7.88 ^b				
24	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	2.59 ^b	7.37 ^b	> 1.00 ^a				

25	—	—	—	1.51 ^b	3.59 ^b	8.57 ^b
26	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.82 ^b	3.21 ^b	5.66 ^b
27	—	—	—	1.48 ^b	2.84 ^b	5.42 ^b
28	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.40 ^b	2.76 ^b	5.45 ^b
29	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	2.11 ^c	6.93 ^c	2.57 ^b
30	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	2.14 ^c	6.43 ^c	2.37 ^b
31	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.72 ^c	3.09 ^c	5.56 ^c
32	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	2.02 ^b	4.23 ^b	8.86 ^b
33	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.11 ^b	2.31 ^b	4.81 ^b
34	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.54 ^b	2.88 ^b	5.37 ^b
35	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	7.71 ^c	2.34 ^b	6.02 ^b
36	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.73 ^b	3.51 ^b	7.11 ^b
37	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	3.99 ^c	1.61 ^b	4.02 ^b
38	—	—	—	3.27 ^c	1.27 ^b	3.57 ^b
39	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.65 ^b	3.01 ^b	5.49 ^b
40	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.49 ^b	2.81 ^b	5.30 ^b
41	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	2.83 ^c	1.02 ^b	3.19 ^b
42	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	3.01 ^b	> 1.00 ^a	> 1.00 ^a
43	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.74 ^c	3.19 ^c	5.86 ^c
44	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.57 ^b	3.15 ^b	6.32 ^b
45	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.83 ^c	4.34 ^c	1.08 ^b
46	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.81 ^c	3.83 ^c	8.10 ^c
47	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	2.10 ^c	5.76 ^c	2.05 ^b
48	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.83 ^c	3.91 ^c	8.32 ^c
49	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	4.43 ^c	1.60 ^b	4.00 ^b
50	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.63 ^c	3.04 ^c	5.67 ^c
51	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.41 ^b	2.74 ^b	5.35 ^b
52	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	9.81 ^c	2.15 ^b	4.63 ^b
53	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	7.97 ^c	2.62 ^b	7.40 ^b
54	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	2.29 ^b	—	—
55	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.30 ^b	2.61 ^b	5.24 ^b
56	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.71 ^b	4.46 ^b	—
57	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	7.98 ^c	2.05 ^b	4.53 ^b
58	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	3.05 ^c	1.02 ^b	3.20 ^b
59	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.56 ^b	2.92 ^b	5.44 ^b
60	> 1.00 ^a	> 1.00 ^a	> 1.00 ^a	1.94 ^c	4.21 ^c	9.12 ^c

^a × 10⁻⁴; ^b × 10⁻⁵; ^c × 10⁻⁶; ^d × 10⁻⁷ M.

GI₅₀, TGI, and LC₅₀ determined by interpolation, representing the drug concentrations corresponding to PG = +50, 0, and -50 (50% growth inhibition, total growth inhibition, and 50% loss of cells, respectively). It should be noted that the latter parameter does not coincide with the conventional LC₅₀ value, since these drug concentrations do not result in the loss of nontumor cells. In some cases, when the characteristic quantities cannot be obtained by interpolation, the parameters are represented by values above the maximum concentration [14].

The screening method used in this study is standard. Since the maximum concentrations (LC₅₀) determined by

this method for some well-known antitumor drugs (adriamycin analogs) such as zorubicin (1.25×10^{-4} M), daunorubicin (5.0×10^{-5} M), and piroxantrone (2.5×10^{-4} M) coincide with the reported values [15] and are always reproduced, reference to other drugs is not necessary.

RESULTS AND DISCUSSION

The results of our experiments showed that the antitumor activity level of some of the tested compounds, such as

pyrrolines Ia and II and tetrahydropyridine VIIa (see Table 1), is close to that of the well-known drugs mentioned above. An analysis of the behavior of compounds belonging to various classes indicates that pyrrolidines I possess moderate antitumor activity. Substitution of an alkyl fragment for aromatic significantly reduces activity with respect to all of the tumor cell lines studied. At the same time, replacing the aromatic radical R¹ with an azomethine fragment is not as pronounced. Note also that using an electron-donor substituent R¹ in position 4 and an electron-acceptor R increases the cytotoxic effect of pyrrolines I. On the whole, the activity of all pyrrolines is more pronounced with respect to leukemia, melanoma, and cancers of the breast, kidney, and rectum, although there are activity manifestations in some other tumor cell lines as well. The maximum antitumor activity was observed for compounds Ia and II.

Upon going to pyrroles II, the overall antitumor activity exhibits a decrease. This drop is especially manifested in compounds IIa and IIo, representing the derivatives of pyrrolines Ia and II, respectively. The action of compounds IIa and IIi amounts to some suppression of the tumor growth, while the cytotoxic effect is virtually absent. Note that activity of the N-unsubstituted pyrrole III does not exceed the average level typical of compounds II.

Dioxabicyclic derivatives IV unsubstituted at position 8 (compound IVI) exhibit no antitumor properties at all. The activity markedly increases upon passage to methyl-substituted analogs IVe – IVk; these compounds are capable of suppressing the tumor cell growth and exhibit cytotoxic action (with LC₅₀ up to 4.78×10^{-5} M) with respect to some cell subgroups representing rectal cancer (COLO 205, HCC-2998, and HCT-15), melanoma (M-14, SK-MEL-5), and kidney cancer (CAKI-1, SNI2C). The activity spectrum of tetramethyl-substituted compounds IVa – IVd and IVn expands to include the subgroups of breast cancer (HS 578T and MDA-N, LC₅₀ up to 3.46×10^{-5} M). Similarly to the case of pyrrolidines I and pyrroles II, the presence of an aromatic R² (compounds IVa, IVe – IVg, IVn) generally increases the antitumor activity.

No antitumor activity was found in the triazine derivatives V. Only phenyl-substituted compounds IVd and Ve at maximum concentrations produced a 50% growth inhibition of leukemia cells (CCRF-CEM and K-562 lines, respectively).

Also inactive were compounds VI and VIII. Only compound VIa produced a 50% growth inhibition for the MCF₇

breast cancer cells and compound VIb (both at maximum concentrations) fully inhibited the growth of the CCRF-CEM leukemia cells.

Among the tetrahydropyridine derivatives VII, only compound VIIa is worth noting for its comparatively high antitumor activity with respect to all of the tumor cell lines studied (except for leukemia, where only suppression of the cell growth was observed). Remarkably, the tumor cells are affected for the most part at small concentrations of this compound. Repeated experiments allowed this compound to be selected also for subsequent testing *in vivo*.

Thus, the results of *in vitro* screening showed evidence of the antitumor activity in 2-pyrroline-3,4,4-tricarbonitriles (I) and 1,2,3,4-tetrahydropyridine-3,3,4,4-tetracarbonitriles (VII).

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