

(Reviewer's self-reminder for trend test: Rat, Male, Combined control, combined tumor types)

glandularstomach(fundus	(15)	IN 92-103	1	0	0	0	1	1	0.000	0.000	0.000
neuroendocrinetumor/B+M	(150c)	IN 92-103	2	6	7	14	11	11			
			IN 104-109	1	0	0	0	3	6			
			IN 104-109	2	32	26	20	26	16			
Spontaneous tumor pct: <= 1% in ctrl.	-	Total	-	-	0	0	0	4	7	(P<0.025)		

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Dose-Tumor Trend Analysis of Female Rats

Analysis of Carcinogenic Potential in Female Rat

Test of Dose-Response (Tumor) Positive Linear Trend

Study No. FISCHERRAT

Run Date & Time: April 20, 1999 (14:08)

Source: e:\panto\f\c\XAnimalX.txt

Note: Dose Levels Included: CTRL1 CTRL2 LOW MED HIGH (0 0 5 15 50)
 Missing value in Tumor-Caused Death is treated as tumor not causing death
 Tumor Type: IN: Incidental (nonfatal) tumor, FA: Fatal tumor.

(Reviewer's self-reminder for trend test: Rat, Female, Combined control, separate tumor types)

ORGAN/TISSUE NAME AND TUMOR NAME	(ORG#) (TMR#)	TUMOR TIME TYPES STRATA	ROW NO.	2x2 CONTINGENCY -----TABLES-----	EXACT ASYMP PROB	ASYMP PROB	PROB /CONT CORR
adrenals	(1) IN 53-78	1	0 1 0 0 0	0.353	0.340	0.344
medullarytumor/B	(0101) IN 53-78	2	2 6 6 3 8			
		IN 104-109	1	2 1 1 1 2			
		IN 104-109	2	27 17 12 14 13			
Spontaneous tumor pct: 4%	in ctrl.	- Total	-	2 2 1 1 2			
adrenals	(1) IN 92-103	1	0 0 0 0 1	0.624	0.598	0.603
corticalcelladenoma	(0102) IN 92-103	2	7 3 6 6 4			
		IN 104-109	1	4 0 0 0 0			
		IN 104-109	2	25 18 13 15 15			
Spontaneous tumor pct: 4%	in ctrl.	- Total	-	4 0 0 0 1			
adrenals	(1) IN 104-109	1	0 1 0 0 0	1.000	0.739	0.748
corticalcellcarcinoma	(0204) IN 104-109	2	29 17 13 15 15			
Spontaneous tumor pct: <= 1%	in ctrl.	- Total	-	0 1 0 0 0			
eyes	(11) IN 104-109	1	0 1 0 0 0	1.000	0.741	0.750
leiomyoma	(1201) IN 104-109	2	29 16 13 15 15			
Spontaneous tumor pct: <= 1%	in ctrl.	- Total	-	0 1 0 0 0			
forestomach	(13) IN 104-109	1	0 1 0 0 0	1.000	0.739	0.748
squamouscellpapilloma	(1301) IN 104-109	2	29 17 13 15 15			
Spontaneous tumor pct: <= 1%	in ctrl.	- Total	-	0 1 0 0 0			
glandularstomach(fundus	(15) IN 0-52	1	0 0 0 0 1	0.009	0.004	0.004
neuroendocrinetumor/B	(1501) IN 0-52	2	7 18 22 21 20			
		IN 79-91	1	0 0 0 1 1			
		IN 79-91	2	3 4 3 4 0			
		IN 92-103	1	0 0 0 2 0			
		IN 92-103	2	8 3 6 4 5			
		IN 104-109	1	0 0 2 6 2			
		IN 104-109	2	29 18 11 9 13			
Spontaneous tumor pct: <= 1%	in ctrl.	- Total	-	0 0 2 9 4			(P<0.025)
glandularstomach(fundus	(15) IN 92-103	1	0 0 0 1 2	0.027	0.014	0.015
neuroendocrinetumor/M	(1502) IN 92-103	2	8 3 6 5 3			
		IN 104-109	1	0 0 2 2 1			
		IN 104-109	2	29 18 11 13 14			
Spontaneous tumor pct: <= 1%	in ctrl.	- Total	-	0 0 2 3 3			
mammarygland	(25) IN 104-109	1	1 1 1 1 0	0.714	0.770	0.774
fibroadenoma	(2501) IN 104-109	2	28 17 12 14 15			
Spontaneous tumor pct: 2%	in ctrl.	- Total	-	1 1 1 1 0			
mammarygland	(25) IN 104-109	1	2 0 0 0 0	1.000	0.819	0.824
adenocarcinoma	(2505) IN 104-109	2	27 18 13 15 15			
Spontaneous tumor pct: 2%	in ctrl.	- Total	-	2 0 0 0 0			
mammarygland	(25) IN 104-109	1	0 0 0 1 1	0.082	0.049	0.051
adenoma	(2506) IN 104-109	2	29 18 13 14 14			
Spontaneous tumor pct: <= 1%	in ctrl.	- Total	-	0 0 0 1 1			

pancreas	(27)	IN 79-91	1	0	0	0	1	0	0.400	0.326	0.341
isletcelladenocarcinoma	(2702)	IN 79-91	2	2	4	3	4	1			
Spontaneous tumor pct: <= 1% in ctrl.	-	Total	-	-	0	0	0	1	0			
parathyroids	(28)	IN 104-109	1	0	0	0	0	1	0.176	0.018	0.020
adenoma	(2801)	IN 104-109	2	29	17	12	12	14			
Spontaneous tumor pct: <= 1% in ctrl.	-	Total	-	-	0	0	0	0	1			
pituitary	(30)	IN 0-52	1	0	1	0	0	0	0.176	0.170	0.171
parsdistalisadenoma	(3001)	IN 0-52	2	6	12	15	18	15			
			IN 79-91	1	1	0	2	2	0			
			IN 79-91	2	0	2	1	2	0			
			IN 92-103	1	1	1	0	1	2			
			IN 92-103	2	6	2	6	5	2			
			IN 104-109	1	17	4	6	3	7			
			IN 104-109	2	12	14	7	12	8			
			FA 68	1	0	0	1	0	0			
			FA 68	2	38	25	22	26	22			
			FA 76	1	0	0	0	0	1			
			FA 76	2	37	24	22	26	20			
			FA 81	1	0	1	0	0	0			
			FA 81	2	37	23	21	26	20			
			FA 91	1	0	0	0	1	1			
			FA 91	2	36	21	19	21	19			
Spontaneous tumor pct: 26% in ctrl.	-	Total	-	-	19	7	9	7	11			
pituitary	(30)	IN 104-109	1	1	0	0	0	1	0.206	0.166	0.170
parsdistalisadenocarcin	(3003)	IN 104-109	2	28	18	13	15	14			
			FA 87	1	0	0	0	1	0			
			FA 87	2	37	22	19	25	20			
Spontaneous tumor pct: <= 1% in ctrl.	-	Total	-	-	1	0	0	1	1			
skin	(36)	IN 0-52	1	0	0	1	0	0	0.707	0.723	0.732
fibroushistiocytoma/B	(3603)	IN 0-52	2	8	18	20	21	21			
Spontaneous tumor pct: <= 1% in ctrl.	-	Total	-	-	0	0	1	0	0			
skin	(36)	IN 104-109	1	0	0	1	2	1	0.201	0.146	0.149
squamouscellcarcinoma	(3606)	IN 104-109	2	29	18	12	12	14			
			FA 93	1	0	0	0	1	0			
			FA 93	2	37	21	18	19	20			
Spontaneous tumor pct: <= 1% in ctrl.	-	Total	-	-	0	0	1	3	1			
skin	(36)	IN 92-103	1	0	0	0	0	1	0.185	0.023	0.024
keratoacanthoma	(3607)	IN 92-103	2	8	3	5	6	4			
Spontaneous tumor pct: <= 1% in ctrl.	-	Total	-	-	0	0	0	0	1			
skin	(36)	IN 104-109	1	0	0	0	0	1	0.168	0.016	0.018
hairfollicletumor/B	(3608)	IN 104-109	2	29	18	13	14	14			
Spontaneous tumor pct: <= 1% in ctrl.	-	Total	-	-	0	0	0	0	1			
thyroids	(41)	IN 92-103	1	1	0	0	0	0	0.498	0.501	0.503
C-celltumor/B	(4101)	IN 92-103	2	6	3	6	5	4			
			IN 104-109	1	6	3	2	4	3			
			IN 104-109	2	23	15	11	11	12			
Spontaneous tumor pct: 10% in ctrl.	-	Total	-	-	7	3	2	4	3			
thyroids	(41)	IN 104-109	1	0	1	0	0	0	1.000	0.739	0.748
folliclecellcarcinoma	(4102)	IN 104-109	2	29	17	13	15	15			
Spontaneous tumor pct: <= 1% in ctrl.	-	Total	-	-	0	1	0	0	0			
thyroids	(41)	IN 104-109	1	2	1	0	1	1	0.446	0.427	0.432
C-celltumor/M	(4201)	IN 104-109	2	27	17	13	14	14			
Spontaneous tumor pct: 3% in ctrl.	-	Total	-	-	2	1	0	1	1			
haematopoeticsystem	(47)	IN 104-109	1	2	0	0	0	0	0.864	0.885	0.887
LGLleukemia	(4701)	IN 104-109	2	27	18	13	15	15			
			FA 45	1	0	0	0	1	0			
			FA 45	2	46	39	32	33	33			
			FA 65	1	0	0	0	1	0			
			FA 65	2	42	28	23	27	24			

FA 74	1	0	1	0	0	0	
FA 74	2	41	25	22	26	23	
FA 85	1	0	1	0	0	0	
FA 85	2	38	23	21	26	21	
FA 90	1	0	0	0	1	0	
FA 90	2	37	21	19	23	21	
FA 93	1	1	0	0	1	0	
FA 93	2	36	21	19	20	20	
FA 95	1	0	0	0	1	0	
FA 95	2	36	20	17	18	20	
FA 96	1	1	0	0	0	0	
FA 96	2	35	20	17	18	20	
FA 98	1	1	0	0	0	0	
FA 98	2	34	20	16	17	19	
FA 99	1	0	0	1	0	0	
FA 99	2	34	20	15	17	19	
FA 100	1	1	0	0	0	0	
FA 100	2	33	20	15	17	18	
FA 101	1	0	1	0	0	0	
FA 101	2	33	18	15	15	18	
FA 102	1	0	0	1	0	1	
FA 102	2	30	18	14	15	17	
FA 103	1	1	0	0	0	0	
FA 103	2	29	18	13	15	16	
Spontaneous tumor pct: 10% in ctrl. - Total	-	7	3	2	5	1	
haematopoeticsystem (47) IN 104-109	1	1	1	1	0	5	0.010 0.005 0.005
lymphoma/leukemia, unclas (4702) IN 104-109	2	28	17	12	15	10	
FA 87	1	0	2	0	0	0	
FA 87	2	38	21	19	26	21	
FA 88	1	0	0	0	1	0	
FA 88	2	38	21	19	24	21	
FA 99	1	0	0	0	0	1	
FA 99	2	34	20	16	17	18	
FA 100	1	0	1	0	2	0	
FA 100	2	34	19	15	15	18	
Spontaneous tumor pct: 5% in ctrl. - Total	-	1	4	1	3	6	
oralcavity (andteeth) (49) IN 79-91	1	0	0	0	1	0	0.433 0.445 0.449
squamouscellcarcinoma (4901) IN 79-91	2	2	4	3	3	1	
IN 92-103	1	1	1	0	0	0	
IN 92-103	2	5	2	5	6	4	
IN 104-109	1	0	0	1	0	0	
IN 104-109	2	29	18	12	15	15	
FA 75	1	0	0	0	0	1	
FA 75	2	41	25	22	26	22	
FA 89	1	1	0	0	0	0	
FA 89	2	37	21	19	24	21	
FA 90	1	0	0	0	1	0	
FA 90	2	37	21	19	23	21	
FA 96	1	0	0	0	0	1	
FA 96	2	36	20	17	18	19	
FA 101	1	2	0	0	0	0	
FA 101	2	31	19	15	15	18	
FA 102	1	0	0	1	0	0	
FA 102	2	30	18	14	15	18	
Spontaneous tumor pct: 5% in ctrl. - Total	-	4	1	2	2	2	
liver (54) IN 92-103	1	1	1	0	0	0	0.100 0.092 0.084
hepatocellularadenoma (5401) IN 92-103	2	7	2	6	6	5	
IN 104-109	1	2	0	0	2	3	
IN 104-109	2	27	18	13	13	12	
Spontaneous tumor pct: 4% in ctrl. - Total	-	3	1	0	2	3	
liver (54) IN 79-91	1	0	0	0	1	0	0.375 0.317 0.321
hepatocellularcarcinoma (5402) IN 79-91	2	3	4	3	4	1	
Spontaneous tumor pct: <= 1% in ctrl. - Total	-	0	0	0	1	0	
uterus/ut.-cervix/vag (60) IN 53-78	1	0	0	0	0	1	0.666 0.655 0.668
polyp (6001) IN 53-78	2	2	7	6	3	7	
IN 79-91	1	0	0	0	1	0	

		IN 79-91	2	3	4	3	4	1	
		IN 92-103	1	3	0	1	3	1	
		IN 92-103	2	5	3	5	3	4	
		IN 104-109	1	6	2	3	2	1	
		IN 104-109	2	23	16	10	13	14	
Spontaneous tumor pct: 11%	in ctrl.	- Total	-	9	2	4	6	3	
uterus/ut.-cervix/vag	(60) IN 104-109	1	0	0	1	0	0	0.477 0.642 0.652
granularcelltumor	(6002) IN 104-109	2	29	18	12	15	15	
Spontaneous tumor pct: <= 1%	in ctrl.	- Total	-	0	0	1	0	0	

APPEARS THIS WAY
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(Reviewer's self-reminder for trend test: Rat, Female, Combined control, combined tumor types)

glandularstomach(fundus	(15)	IN 0-52	1	0	0	0	0	1	
neuroendocrinetumor/B+M	(150c)	IN 0-52	2	7	18	22	21	20	0.000 0.000 0.000
			IN 79-91	1	0	0	0	1	1	
			IN 79-91	2	3	4	3	4	0	
			IN 92-103	1	0	0	0	3	2	
			IN 92-103	2	8	3	6	3	3	
			IN 104-109	1	0	0	4	8	3	
			IN 104-109	2	29	18	9	7	12	
Spontaneous tumor pct: <= 1% in ctrl.	-	Total	-	-	0	0	4	12	7	(P<0.025)

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Appendix 2

Additional Trend Tests

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StatXact-3 Output
 Date: Tuesday, May 4, 1999
 Time: 11:2:20

>>> TC PE/EX/PW

Datafile: <new>

PERMUTATION TEST
 [1 2 by 5 informative tables and sum of scores from row <row1 >]

Summary of Exact distribution of PERMUTATION statistic:

<u>Min</u>	<u>Max</u>	Mean	Std-dev	Observed	Standardized
		47.43	34.47	115.0	1.960

Asymptotic Inference:

One-sided p-value: Pr (Test Statistic .GE. Observed) = 0.0250
 Two-sided p-value: 2 * One-sided = 0.0500

Exact Inference:

One-sided p-value: Pr (Test Statistic .GE. Observed) = 0.0448
 Pr (Test Statistic .EQ. Observed) = 0.0316
 Two-sided p-value: Pr (| Test Statistic - Mean |
 .GE. | Observed - Mean |) = 0.0448
 Two-sided p-value: 2*One-Sided = 0.0897

Power Estimation:

Alpha = 0.05000
 Beta = 20.00
 Asymptotic Power = 1.000
 Exact Power = 1.000

Elapsed Time is 0:0:0.22

>>> TC PE/EX/PW

Datafile: <new>

PERMUTATION TEST
 [1 2 by 5 informative tables and sum of scores from row <row1 >]

Summary of Exact distribution of PERMUTATION statistic:

<u>Min</u>	<u>Max</u>	Mean	Std-dev	Observed	Standardized
		42.00	32.46	115.0	2.249

Asymptotic Inference:

One-sided p-value: Pr (Test Statistic .GE. Observed) = 0.0123
 Two-sided p-value: 2 * One-sided = 0.0245

Exact Inference:

One-sided p-value: Pr (Test Statistic .GE. Observed) = 0.0314
 Pr (Test Statistic .EQ. Observed) = 0.0238
 Two-sided p-value: Pr (| Test Statistic - Mean |
 .GE. | Observed - Mean |) = 0.0314
 Two-sided p-value: 2*One-Sided = 0.0628

Power Estimation:

Alpha = 0.05000
 Beta = 20.00
 Asymptotic Power = 1.000
 Exact Power = 1.000

Elapsed Time is 0:0:0.16

APPEARS THIS WAY
ON ORIGINAL