Rapamycin-related lymphoma (multiple organs) was a prominent cause for early death in female mice. The overall lymphoma incidence rates were statistically significant in analyses conducted by the sponsor and the Reviewer from the Division of Biometrics (refer to attached statistical review). Increased lymphoma incident rates were observed in mice with other immunosuppressants such as cyclosporine and azathioprine. Immunosuppressant therapy is also associated with increased incidences of lymphoma in human subjects and the sponsor acknowledges that rapamycin may act similarly in patients undergoing transplant therapy.

Comments

The current study was inadequate for assessing the carcinogenic activity in male mice due to the toxicity of rapamycin at all dose levels and the premature termination of the study at Week 26. The study was also problematic for female mice because the original high dose level of 50 mg/kg was reduced at Week 31 to 6 mg/kg. An adequate dose-response analysis cannot be made because of this alteration in dose levels. A rodent carcinogenicity study needs to have at least three discreet dose levels of the test compound for proper dose-response analyses to be made. The current study has two discreet levels, 12.5 and 25 mg/kg, and a hybrid level (50 / 6 mg/kg) that cannot be accurately related to either the 12.5 or 25 mg/kg dose. The sponsor indicated that a second carcinogenicity study with mice was initiated and the final report should be issued to FDA by March, 2000.

Evaluation and Conclusion

The rat carcinogenic study was adequate for evaluating the tumorigenic potential of rapamycin in male and female rats. However, the sponsor pooled the histopathological data from the two control groups for each sex and then conducted statistical analyses for neoplastic and non-neoplastic lesions. The two control groups for each sex should have been kept separate and statistically analyzed as two distinct zero-level controls in conjuction with the three separate rapamycin dose groups. Although keeping the control histopathological incidence rates separate for the two control groups is the preferred procedure for statistical analysis of the tumorigenic incidence rate, pooling the control data for this specific study had no impact upon the final conclusions.

Rapamycin dosing resulted in testicular interstitial cell adenomas in male rats. In a previous 52-week study with male rats rapamycin caused testicular interstitial cell hyperplasia, a depression in testosterone levels, and an elevation in luteinizing hormone levels. The sponsor proposed that the interstitial cell hyperplasia and subsequent progression to interstitial cell adenoma resulted from chronic overproduction of luteinizing hormone. The sponsor further argued that these effects in rats may not be applicable to human males due to the reduced number of androgen receptors in human interstitial cells compared to rats. The proposed mechanism by the sponsor is plausible, however, the sponsor would need to develop additional and definitive mechanism of action data with rapamycin in order to provide appropriate experimental proof. Included

in this experimental package would be appropriate receptor studies with human testicular cells. The testicular data, both neoplastic and non-neoplastic, and the non-neoplastic histopathology observed in seminal vesicles, epididymides, and prostate gland are reflective of toxicological effects that appear to be independent of the immunosuppressive activity of rapamycin.

Fibroma of the cervix was observed in female rats and was statistically significant at the intermediate dose only (0.1 mg/kg). The absence of a dose response and the low incidence rate reduce the biolgical relevance of this observation [redacted] Other observed tumors in males and females were ultimately determined to be not statistically significant.

The mouse carcinogenicity study was not adequate for male mice due to the unscheduled termination of the study during Week 29. Results from the male mice were not evaluated in the current review. Female mice were dosed for 86 weeks, the study was terminated during Week 86, due to mortality in the rapamycin dosed animals. In addition, the initial high dose level of 50 mg/kg was reduced to 6 mg/kg during Week 31, because of adverse clinical effects. From the perspective of study duration (86 weeks) and number of animals surviving to the terminal sacrifice, the study was adequate for evaluating the tumorigenic activity of rapamycin in female mice. However, an appropriate dose response cannot be conducted because of the hybrid 50 mg/kg to 6 mg/kg dose group. It is not possible, based upon available data, to properly relate this hybrid dose level to the other rapamycin dose levels (12.5 and 25 mg/kg). The sponsor recognized these deficiencies and conducted a second carcinogenicity study in mice. The final report for the second mouse carcinogenicity study should be submitted by March, 2000.

Despite the deficiencies, rapamycin dosing clearly resulted in statistically significant levels of multisystemic lymphomas in the female mice. This observation is not unexpected as other immunosuppressive drugs caused elevated incidences of lymphomas in mice. Immunosuppressant therapy in transplant patients can also result in lymphomas. Also of interest in female mice was the non-neoplastic incidence of uterine atrophy that resulted from rapamycin dosing. A no-effect level for this lesion was not established and the underlying toxicological mechanism is apparently not due to the immunosuppressive activity of rapamycin. Additional studies to clarify the underlying mechanism of action for uterine atrophy by rapamycin may be useful.

Keywords: Immunosuppressant, Rapamycin, Rodent Carcinogenicity

Attachments:

[redacted]

3) Statistical Review and Evaluation: Carcinogenicity, 6/22/99.

/S/ 8/24/99

Stephen G. Hundley, Ph.D
Pharmacology Reviewer

Concurrences:
HFD-590/R.Albrecht/DDDir
HFD-590/ K.Hastings/TL

Disk:
HFD-590/K.Hastings

cc:
HFD-590/Original NDA
HFD-590/Division File
HFD-345
HFD-590/Pharm/S.Kunder
HFD-590/Pharm/S.Hundley
HFD-590/CSO/M.Bacho
HFD-590/Micro/S.Bala
HFD-590/Chem/M.Seggel
HFD-590/MO/R.Tiernan
HFD-590/Stat/N.Silliman
HFD-590/Biopharm

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ON ORIGINAL

12 pages

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TRADE Secret/
confidential/
commercial

STATISTICAL REVIEW AND EVALUATION
CARCINOGENICITY

NDA #:	21-083
Name of Drug:	Rapamune (sirolimus) oral solution
Applicant:	Wyeth Ayerst
Documents Reviewed:	Volumes 51-59 and electronic data submission
Statistical Reviewer:	Nancy Silliman, Ph.D.
Pharmacologist:	Steve Kunder, Ph.D. and Steve Hundley, Ph.D.
Project Manager:	Matthew Bacho
Key Words:	Peto, trend test, pairwise comparisons, adjusted p-values, adjusted α-levels

Summary of Review

- In this review, a tumor is declared "rare" if the incidence in the control group is ≤1% and "common" if the incidence in the control group is >1%.
- For positive linear trend analyses, "rare" tumors are tested using a significance level of 0.025; "common" tumors are tested using a significance level of 0.005.
- For pairwise comparisons, "rare" tumors are tested using a significance level of 0.05, while "common" tumors are tested using a significance level of 0.01.
- Problems related to the maximum tolerated dose (MTD) being exceeded were seen in the mouse study. The male portion of this study was terminated early after 29 weeks, the female portion of this study was terminated early after 86 weeks, and the female high dose group was modified from receiving the highest dose to actually receiving the lowest dose. As a result, no conclusions are drawn in this review about possible carcinogenic effects in male mice (they were not followed long enough for any conclusions to be drawn). The pharmacologist will have to determine whether female mice were followed for an adequate length of time. In addition, the trend tests for female mice could only compare the control, low, and medium dose female mice. The pharmacologist will have to determine whether a wide enough range of doses were studied for female mice.
- In the female mice, a positive dose mortality trend was detected in survival (i.e., mortality was found to increase with dose). No dose mortality trend was detected in the rat study. The trend tests used in this review which look at tumor incidence adjust for differences in intercurrent mortality.
- The percent loss in group mean body weights compared to controls was greater than 10% in the medium and high dose male rats (15% and 22%, respectively), and also in the low, medium, and "high" dose female mice (14%, 21%, and 16%, respectively). The pharmacologist will have to determine if these dose groups can be considered appropriate for the rat study, i.e., close to MTD.

- The only significant trend test found in the rat study was for the incidence of testicular interstitial cell adenomas (p=0.004). Pairwise comparisons for this tumor were not significant in the low and medium dose male groups (p=0.974 and p=0.063, respectively), but were marginally significant in the high dose male group (p=0.013; the significance level used here is 0.01 as this tumor was seen in 5% of the control group and is thus classified as "common").
- The only significant trend test found in the female mice (recall that these only compare control, low, and medium dose groups) was for the incidence of lymphoma (p=0.002; lymphoma occurred at a rate of 5% in the control group and was thus considered "common"). Pairwise comparisons for lymphoma were found to be significant in all female mice dose groups (p=0.003 for the low dose group, p=0.003 for the medium dose group, and p<0.001 for the "high" dose group). No other pairwise comparisons for the "high" dose female group were found to be significant.

I. Background

Two animal carcinogenicity studies (Study 103 in rats and Study 104 in mice) were included in this NDA submission. Rapamune, an immunosuppressant, was administered orally by gavage once daily in both studies to evaluate its carcinogenic potential.

In study 103, male and female CD VAF rats were dosed for 104 weeks at dosages of 0, 0, 0.05, 0.1, and 0.2 mg/kg/day. There were 65 rats/sex in each of the two control groups and the low, medium, and high dose groups. Control groups were combined for analysis. Approximately 55 tissues from each animal were examined grossly and microscopically.

In study 104, male and female CD-1 VAF mice were dosed at 0, 0, 12.5, 25, and 50 (lowered to 6 mg/kg/day in the females at week 31) mg/kg/day for 29 (males) or 86 (females) weeks. There were 60 mice/sex in the first control group, 75 mice/sex in the second control group, and 75 mice/sex in each of the low, medium, and high dose groups. Control groups were combined for analysis. Approximately 55 tissues were examined grossly and microscopically from all females. Only certain tissues were examined from the various male groups microscopically (all were examined in the first control group and the high dose group, and about 8 were examined from the low and medium dose groups). Normally this would restrict our conclusions from the trend test for males to only those tissues that were examined microscopically for all male animals. However, this point is moot since the study was unable to follow male mice long enough to assess carcinogenic potential in the male mice (see below).

The sponsor notes that while the original intent of Study 104 was to assess the carcinogenic potential of Rapamune, the health status of the mice was compromised by skin lesions, especially in the male mice. It was determined that all dosed groups in the males had exceeded the maximum tolerated dose (MTD), as had the high dose group in the females. As a result, the male portion of the study was terminated after 29 weeks and the female portion of the study was modified by lowering the high dose group (50 mg/kg/day) to approximately half of what the low dose group was receiving (i.e., 6 mg/kg/day) at week 31. The female portion of the study was also terminated early at 86 weeks due to similar problems with the low and medium dose groups. Thus, the study failed to assess carcinogenic potential in male mice but still provides some information about carcinogenic potential in female mice, although not as much as originally planned due to the problems with the high dose group and early termination. It is unclear whether the problems with skin lesions were related to the animals (the sponsor notes that such lesions have been seen in their and other laboratories with CD-1 mice but at a much

lower incidence and severity) or to Rapamune which is an immunosuppressant (incidence of the lesions appeared to be dose-related).

II. Methods

For each species and sex, the sponsor and reviewer analyzed palpable, nonpalpable-lethal, and nonpalpable-nonlethal tumors separately, then combined the results using Peto et al.[1] procedures. For a particular tumor type of interest, the incidence data can be summarized in a 2xD table, where D is the number of dose groups. The first row contains the number of animals with the tumor of interest, and the second row contains the number of animals without the tumor. However, this summary table can be misleading. If the toxicity of the drug causes animals to die early by some non-cancer related cause, fewer animals will be at rish for tumors in the higher dose groups. Thus, even if the drug also increases the tumor rate, the overall incidence of that tumor in the high dose groups may be smaller than in the control groups. To adjust for the effect that potential differential mortality between the dose groups has on tumor occurrence, the Peto prevalence method breaks up study time into several discrete intervals. The intervals used in the rat study were weeks 1-52, weeks 53-78, weeks 79-91, weeks 92-104, and terminal sacrifice. The intervals used for the female mice were weeks 1-52, weeks 53-78, weeks 79-86, and terminal sacrifice. No analysis was performed by either the reviewer or the sponsor for male mice. The data can thus be represented by several 2xD tables, one for each time interval. Note that Peto et al. point out that "the effects of differences in longevity on numbers of tumor-bearing animals can be very substantial, and so, whether or not they appear to be they should routinely be corrected for when presenting experimental results."

The dose groups can also be assigned weights in the statistical analysis to test various hypotheses. For example, using weights of (0, 1, ..., D) gives the trend test which is sensitive to a linear dose effect. Using equal weights (1, 1, ..., 1) gives a test of association between dose and tumor rate without specifying the form of the relationship. Weight can also be set equal to the actual doses given. Finally, choosing weights close to the actual biological effect of the doses will result in the most sensitive test, but in practice this effect is not known. Linear weights or dose weights are often used. The sponsor used both linear and dose weights in their analysis. As results were similar between the two, this reviewer used dose weights.

For the tumor type of interest, each tumor is classified as "fatal", "non-fatal", or "mortality independent tumors". P-values are calculated for the three classes separately, and then combined to yield a single p-value for the tumor type. Both exact and asymptotic p-values are calculated for most tumor types (statisticians in CDER routinely use the exact method to test for positive linear trend when the number of total tumors across treatment groups is 10 or smaller).

One-sided p-values may be more appropriate than two-sided p-values, since they are more conservative and we are only interested in whether increased doses *increase* tumor incidence. One-sided p-values are reported in this review.

As so many sex/species/organ/tumor type combinations are tested, a simple application of a 0.05 decision rule does not appropriately control the overall false positive rate. It has been

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[1] Peto R, Pike MC, Day NE, Gray RG, Lee PN, Parish S, Peto J, Richards S, and Wahrendorf J (1980). "Guidelines for Simple, Sensitive Significance Tests for Carcinogenic Effects in Long-term Animal Experiments", in Long-term and Short-term Screening Assays for Carcinogens: An Critical Appraisal, World Health Organization.

suggested by Drs. Lin and Rahman[2] that if the tumor is "rare" the cutoff should be 0.025 and if the tumor is "common" the cutoff should be 0.005. Tumors are defined as rare or common using historical control data or the control group in the study being analyzed (in this review, the control group is used). The usual practice at FDA is to classify a tumor as common if it occurs in the control group at an incidence of greater than 1%. Using simulation tests on CD-1 rats and CD(BR) mice, Lin and Rahman found that the overall false positive rate resulting from the use of the α–levels 0.025 and 0.005 in the tests for linear trend in a two-species-two-sex study is about 10%. These false-positive rates are judged by the Center for Drug Evaluation and Research as the most appropriate in a regulatory setting.

For pairwise comparisons, the levels of significance that are used are 0.05 for rare tumors and 0.01 for common tumors.

III. Analysis

Rat Study 103

Both the reviewer's and the sponsor's analyses used the Peto et al. procedures described above. Reviewer analyses for male rats (exact and asymptotic trend tests) can be found in Appendix 1. Reviewer analyses for female rats (exact and asymptotic trend tests) are given in Appendix 2.

As described above, for the trend test Drs. Lin and Rahman suggest that if a tumor is "rare" it be tested using a significance level of 0.025. "Common" tumors are to be tested using a significance level of 0.005. Using this rule, the only significant trend test found in the rat study was for the incidence of testicular interstitial cell adenomas (p=0.004). Pairwise comparisons for this tumor were not significant in the low and medium dose male groups (p=0.974 and p=0.063, respectively), but were marginally significant in the high dose male group (p=0.013; the significance level used here, as suggested by Drs. Lin and Rahman, is 0.01 as this tumor was seen in 5% of the control group and is thus classified as "common"). Note that none of the testicular interstitial cell adenomas were classified by the sponsor as fatal (2 of the high dose males who developed these tumors had cause of death coded as "undetermined"; the remaining animals who developed these tumors had cause of death coded as "tumor did not cause death").

No dose mortality trend in survival was detected in the rat study. However, as suggested by Peto et al., the trend tests used in this review which look at tumor incidence still adjust for differences in intercurrent mortality. Using the rule of thumb suggested in the draft Guidance for Industry[3], exposure to the drug can be considered adequate as more than 20-30 animals were still alive at 80-90 weeks for both male and female high dose groups.

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[2] Lin KK and Rahman MA (1998), "Overall False Positive Rates in Tests for Linear Trend in Tumor Incidence in Animal Carcinogenicity Studies of New Drugs", *Journal of Biopharmaceutical Statistics* 8(1), pgs. 1-15.

[3] Draft Guidance for Industry, "On Statistical Aspects of Design, Analysis, and Interpretation of Animal Carcinogenicity Studies", Center for Drug Evaluation and Research, Food and Drug Administration, Rockville, Maryland.

The percent loss in group mean body weights compared to controls was greater than 10% in the medium and high dose male rats (15% and 22%, respectively). The pharmacologist will have to determine if these dose groups received doses close to MTD.

Mouse Study 104

The sponsor's analyses used the Peto et al. procedures described above. As the reviewer validated the sponsor's analyses in the rat study (i.e., reviewer results were found to be the same as sponsor results), and the sponsor performed the correct analyses for the mouse study, this reviewer did not repeat the analyses. Hence, conclusions in this review for the mouse study are based on sponsor results.

Recall that problems related to the maximum tolerated dose (MTD) being exceeded were seen in the mouse study. The male portion of this study was terminated early after 29 weeks, the female portion of this study was terminated early after 86 weeks, and the female high dose group was modified from receiving the highest dose to actually receiving the lowest dose. As a result, no conclusions are drawn in this review about possible carcinogenic effects in male mice (they were not followed long enough for any conclusions to be drawn). The pharmacologist will have to determine whether female mice were followed for an adequate length of time. In addition, the trend tests for female mice could only compare the control, low, and medium dose female mice. The pharmacologist will have to determine whether a wide enough range of doses were studied for female mice.

Again using the rules for significance levels suggested by Drs. Lin and Rahman, the only significant trend test found in the female mice was for the incidence of lymphoma ($p=0.002$; lymphoma occurred at a rate of 5% in the control group and was thus considered "common"). Pairwise comparisons for lymphoma were found to be significant in all female mice dose groups ($p=0.003$ for the low dose group, $p=0.003$ for the medium dose group, and $p<0.001$ for the "high" dose group). Overall, approximately 83% of these tumors were classified by the sponsor as fatal (6/7=86% of the control group, 7/10=70% of the low dose group, 8/9=89% of the medium dose group, and 12/14=86% of the "high" dose group who developed this tumor had cause of death coded as "tumor caused death"; the remaining animals with this tumor had cause of death coded as "tumor did not cause death"; no significant differences were found in cause of death between dose groups: Fisher's exact two-sided $p=0.80$). No other pairwise comparisons for the "high" dose female group were found to be significant.

In the female mice, a positive dose mortality trend was detected in survival (i.e., mortality was found to increase with dose; two-sided $p=0.003$ for the linear trend test comparing control, low, and medium dose groups). Survival was also decreased in the "high" dose females compared to controls (two-sided $p<0.001$ for the pairwise comparison between "high" dose and control). The trend tests used in this review which look at tumor incidence adjust for differences in intercurrent mortality. Using the rule of thumb suggested in the draft Guidance for Industry (see above reference), exposure to the drug can be considered adequate as more than 20-30 animals were still alive at 80-90 weeks for the female medium and "high" dose groups (note that the medium dose group is probably the most appropriate to use here).

The percent loss in group mean body weights compared to controls was greater than 10% in the low, medium, and "high" dose female mice (14%, 21%, and 16%, respectively). The pharmacologist will have to determine if these dose groups can be considered close to MTD.

IV. Discussion

As is common practice in the Center for Drug Evaluation and Research, in this review a tumor is declared "rare" if the incidence in the control group is ≤1% and "common" if the incidence in the control group is >1%. As suggested by Drs. Lin and Rahman, for positive linear trend analyses, "rare" tumors are tested using a significance level of 0.025, while "common" tumors are tested using a significance level of 0.005. For pairwise comparisons, "rare" tumors are tested using a significance level of 0.05, and "common" tumors are tested using a significance level of 0.01.

Problems related to the maximum tolerated dose (MTD) being exceeded were seen in the mouse study. The male portion of this study was terminated early after 29 weeks, the female portion of this study was terminated early after 86 weeks, and the female high dose group was modified from receiving the highest dose to actually receiving the lowest dose. As a result, no conclusions are drawn in this review about possible carcinogenic effects in male mice (they were not followed long enough for any conclusions to be drawn). The pharmacologist will have to determine whether female mice were followed for an adequate length of time. In addition, the trend tests for female mice could only compare the control, low, and medium dose female mice. The pharmacologist will have to determine whether a wide enough range of doses were studied for female mice.

In the female mice, a positive dose mortality trend was detected in survival (i.e., mortality was found to increase with dose). No dose mortality trend was detected in the rat study. The trend tests used in this review which look at a positive trend in tumor incidence adjust for differences in intercurrent mortality.

The percent loss in group mean body weights compared to controls was greater than 10% in the medium and high dose male rats (15% and 22%, respectively), and also in the low, medium, and "high" dose female mice (14%, 21%, and 16%, respectively). The pharmacologist will have to determine if these dose groups can be considered close to MTD.

The only significant trend test found in the rat study was for the incidence of testicular interstitial cell adenomas (p=0.004). Pairwise comparisons for this tumor were not significant in the low and medium dose male groups (p=0.974 and p=0.063, respectively), but were marginally significant in the high dose male group (p=0.013; the significance level used here is 0.01 as this tumor was seen in 5% of the control group and is thus classified as "common"). Note that none of these tumors were classified by the sponsor as fatal (2 of the high dose males who developed these tumors had cause of death coded as "undetermined"; the remaining animals who developed these tumors had cause of death coded as "tumor did not cause death").

The only significant trend test found in the female mice (recall that these only compare control, low, and medium dose groups) was for the incidence of lymphoma (p=0.002; lymphoma occurred at a rate of 5% in the control group and was thus considered "common"). Pairwise comparisons for lymphoma were found to be significant in all female mice dose groups (p=0.003 for the low dose group, p=0.003 for the medium dose group, and p<0.001 for the "high" dose group). Overall, approximately 83% of these tumors were classified by the sponsor as fatal (6/7=86% of the control group, 7/10=70% of the low dose group, 8/9=89% of the medium dose group, and 12/14=86% of the "high" dose group who developed this tumor had cause of death coded as "tumor caused death"; the remaining animals with this tumor had cause of death coded as "tumor did not cause death"; no significant differences were found in cause of death between dose groups: Fisher's exact two-sided p=0.80). No other pairwise comparisons for the "high" dose female group were found to be significant.

/S/ 6/22/99

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/S/

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Orig. NDA #21-083
HFD-590
HFD-590/Dr. Goldberger
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HFD-590/Dr. Cavaille-Coll
HFD-590/Dr. Tiernan
HFD-590/Mr. Bacho
HFD-725/Dr. Huque
HFD-725/Dr. Silliman
HFD-725/Dr. Dixon
HFD-725/Ms. Shores
This review contains 30 pages (including appendices).

Appendix 1: Analysis of Carcinogenic Potential in Male Rat
Test of Dose-Response (Tumor) Positive Linear Trend
Study No.
Run Date & Time: June 4, 1999 (14:10)
Source: C:\NDAS\RAPCARC\RAT103\st95103.lis

Note: Dose Levels Included: CTRL1 CTRL2 LOW MED HIGH (0 0 0.05 0.1 0.2)
Missing value in Tumor-Caused Death is treated as tumor not causing death
Tumor Type: IN: Incidental (nonfatal) tumor, FA: Fatal tumor.

ORGAN/TISSUE NAME / TUMOR NAME	(ORG#) (TMR#)	TUMOR TYPES	TIME STRATA	ROW NO.	2xC CONTINGENCY TABLES	EXACT PROB	ASYMP PROB	ASYMP PROB /CONT CORR =P(STAT .GE. OBSERVED)
CECUM	(10)	FA	87	1	2 0 0 0 0	1.000	0.921	1.000
X-MALIGNANT LYMPHOMA	(165)	FA	87	2	32 45 41 48 47			
Spontaneous tumor pct: 2% in ctrl. - Total				-	2 0 0 0 0			
CECUM	(10)	FA	105	1	0 0 0 0 1	0.247	0.064	1.000
X-HISTIOCYTIC SARCOMA	(553)	FA	105	2	16 28 18 29 29			
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	0 0 0 0 1			
CERVICAL CORD	(11)	IN	92-103	1	0 1 0 0 0	0.377	0.265	1.000
M-ASTROCYTOMA	(475)	IN	92-103	2	13 11 12 13 8			
		FA	88	1	0 0 0 0 1			
		FA	88	2	36 47 44 53 49			
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	0 1 0 0 1			
CERVICAL CORD	(11)	FA	88	1	0 0 0 0 1	0.217	0.050	1.000
M-MIXED GLIOMA	(479)	FA	88	2	36 47 44 53 49			
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	0 0 0 0 1			
CERVICAL LYMPH	(12)	FA	62	1	0 0 0 0 1	0.602	0.541	1.000
X-MALIGNANT LYMPHOMA	(163)	FA	62	2	65 59 62 59 59			
		FA	84	1	1 0 0 0 0			
		FA	84	2	47 50 48 53 51			
		FA	87	1	1 0 0 0 0			
		FA	87	2	43 48 46 53 50			
Spontaneous tumor pct: 2% in ctrl. - Total				-	2 0 0 0 1			
COLON	(15)	FA	87	1	1 0 0 0 0	1.000	0.844	1.000
X-MALIGNANT LYMPHOMA	(164)	FA	87	2	30 42 39 47 45			
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	1 0 0 0 0			
COLON	(15)	FA	81	1	1 0 0 0 0	1.000	0.834	1.000
M-ADENOCARCINOMA	(263)	FA	81	2	38 47 41 48 48			
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	1 0 0 0 0			
DUODENUM	(16)	IN	92-103	1	1 0 0 0 0	1.000	0.827	1.000
X-MALIGNANT LYMPHOMA	(272)	IN	92-103	2	7 9 10 10 7			
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	1 0 0 0 0			
DUODENUM	(16)	FA	105	1	0 0 0 0 1	0.241	0.061	1.000
X-HISTIOCYTIC SARCOMA	(386)	FA	105	2	16 28 18 29 28			
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	0 0 0 0 1			

EPIDIDYMIDES	(17	)	FA 87	1	1	0	0	0	0	1.000	0.834	1.000
X-MALIGNANT LYMPHOMA	(274	)	FA 87	2	43	48	46	53	50			
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	1	0	0	0	0			
ADRENAL CORTEX	(2	)	FA 70	1	0	0	0	0	1	0.399	0.285	1.000
X-MALIGNANT LYMPHOMA	(226	)	FA 70	2	63	57	60	58	56			
			FA 84	1	1	0	0	0	0			
			FA 84	2	47	50	48	53	51			
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	1	0	0	0	1			
ADRENAL CORTEX	(2	)	IN 53-78	1	0	0	1	0	0	0.662	0.637	0.997
B-CORTICAL ADENOMA	(264	)	IN 53-78	2	9	7	11	6	8			
			IN 79-91	1	2	0	0	0	1			
			IN 79-91	2	19	8	12	2	10			
			IN 92-103	1	0	1	0	0	0			
			IN 92-103	2	13	11	12	13	8			
			IN 104-106	1	1	1	0	0	1			
			IN 104-106	2	20	33	29	39	32			
Spontaneous tumor pct: 4% in ctrl. - Total				-	3	2	1	0	2			
ADRENAL CORTEX	(2	)	IN 92-103	1	1	0	0	0	0	0.352	0.242	1.000
X-HISTIOCYTIC SARCOMA	(325	)	IN 92-103	2	12	12	12	13	8			
			FA 77	1	0	0	0	0	1			
			FA 77	2	58	55	56	54	54			
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	1	0	0	0	1			
ADRENAL CORTEX	(2	)	IN 104-106	1	0	1	0	0	0	1.000	0.847	1.000
M-CORTICAL CARCINOMA	(570	)	IN 104-106	2	21	33	29	39	33			
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	0	1	0	0	0			
HARDERIAN GLAND	(21	)	IN 104-106	1	0	0	1	1	0	0.534	0.512	1.000
M-SQUAMOUS CELL CARCINOMA	(577	)	IN 104-106	2	21	34	28	38	33			
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	0	0	1	1	0			
HEART	(22	)	FA 62	1	0	0	0	0	1	0.754	0.713	1.000
X-MALIGNANT LYMPHOMA	(155	)	FA 62	2	65	59	62	59	59			
			FA 83	1	1	0	0	0	0			
			FA 83	2	49	52	49	53	52			
			FA 84	1	1	0	0	0	0			
			FA 84	2	47	50	48	53	51			
			FA 87	1	1	0	0	0	0			
			FA 87	2	43	48	46	53	50			
Spontaneous tumor pct: 2% in ctrl. - Total				-	3	0	0	0	1			
HEART	(22	)	IN 92-103	1	0	2	0	0	0	0.591	0.559	0.995
M-ENDOCARDIAL SCHWANNOMA	(447	)	IN 92-103	2	13	10	12	13	8			
			IN 104-106	1	1	1	1	1	2			
			IN 104-106	2	20	33	28	38	31			
Spontaneous tumor pct: 3% in ctrl. - Total				-	1	3	1	1	2			
ILEUM	(23	)	FA 87	1	1	0	0	0	0	1.000	0.850	1.000
X-MALIGNANT LYMPHOMA	(166	)	FA 87	2	28	40	38	47	46			
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	1	0	0	0	0			
ILEUM	(23	)	FA 105	1	0	0	0	0	1	0.241	0.061	1.000
X-HISTIOCYTIC SARCOMA	(556	)	FA 105	2	16	28	18	29	28			
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	0	0	0	0	1			

JEJUNUM	(24)	FA 105	1	0	0	0	0	1	0.241	0.061	1.000
X-HISTIOCYTIC SARCOMA	(555)	FA 105	2	16	28	18	29	28			
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	0	0	0	0	1			
KIDNEYS	(25)	FA 62	1	0	0	0	0	1	0.602	0.541	1.000
X-MALIGNANT LYMPHOMA	(161)	FA 62	2	65	59	62	59	59			
		FA 84	1	1	0	0	0	0			
		FA 84	2	47	50	48	53	51			
		FA 87	1	1	0	0	0	0			
		FA 87	2	43	48	46	53	50			
Spontaneous tumor pct: 2% in ctrl. - Total			-	2	0	0	0	1			
KIDNEYS	(25)	IN 92-103	1	0	1	0	0	0	1.000	0.812	1.000
M-LIPOSARCOMA	(35)	IN 92-103	2	13	11	12	13	8			
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	0	1	0	0	0			
KIDNEYS	(25)	FA 105	1	0	0	0	0	1	0.247	0.064	1.000
X-HISTIOCYTIC SARCOMA	(382)	FA 105	2	16	28	18	29	29			
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	0	0	0	0	1			
KIDNEYS	(25)	IN 104-106	1	0	0	0	0	1	0.211	0.048	1.000
B-TUBULAR CELL ADENOMA	(401)	IN 104-106	2	21	34	29	39	32			
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	0	0	0	0	1			
LIVER	(26)	FA 21	1	0	0	0	0	1	0.593	0.559	0.998
X-MALIGNANT LYMPHOMA	(113)	FA 21	2	65	64	65	65	64			
		FA 62	1	0	0	0	0	1			
		FA 62	2	65	59	62	59	59			
		FA 83	1	1	0	0	0	0			
		FA 83	2	49	52	49	53	52			
		FA 84	1	1	0	0	0	0			
		FA 84	2	47	50	48	53	51			
		FA 87	1	2	0	0	0	0			
		FA 87	2	42	48	46	53	50			
Spontaneous tumor pct: 3% in ctrl. - Total			-	4	0	0	0	2			
LIVER	(26)	IN 53-78	1	1	0	0	0	0	0.553	0.528	0.982
B-HEPATOCELLULAR ADENOMA	(159)	IN 53-78	2	8	7	12	6	8			
		IN 79-91	1	2	0	1	0	0			
		IN 79-91	2	18	8	11	2	11			
		IN 104-106	1	1	0	0	3	2			
		IN 104-106	2	20	34	29	36	31			
		FA 84	1	1	0	0	0	0			
		FA 84	2	47	50	48	53	51			
Spontaneous tumor pct: 4% in ctrl. - Total			-	5	0	1	3	2			
LIVER	(26)	IN 92-103	1	1	0	0	0	0	0.115	0.073	0.973
X-HISTIOCYTIC SARCOMA	(322)	IN 92-103	2	12	12	12	13	8			
		FA 77	1	0	0	0	0	1			
		FA 77	2	58	55	56	54	54			
		FA 89	1	0	0	0	1	0			
		FA 89	2	36	47	44	52	48			
		FA 105	1	0	0	0	0	1			
		FA 105	2	16	28	18	29	29			
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	1	0	0	1	2			

LUMBAR CORD	(27	)	FA 84	1	1	0	0	0	0	1.000	0.830	1.000
X-MALIGNANT LYMPHOMA	(225	)	FA 84	2	47	49	48	53	51			
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	1	0	0	0	0			
LUMBAR CORD	(27	)	IN 104-106	1	0	0	0	0	1	0.212	0.049	1.000
M-ASTROCYTOMA	(477	)	IN 104-106	2	21	33	29	39	32			
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	0	0	0	0	1			
LUNG	(29	)	FA 62	1	0	0	0	0	1	0.596	0.534	1.000
X-MALIGNANT LYMPHOMA	(154	)	FA 62	2	65	59	62	59	59			
			FA 83	1	1	0	0	0	0			
			FA 83	2	49	52	49	53	52			
			FA 84	1	1	0	0	0	0			
			FA 84	2	47	50	48	53	51			
Spontaneous tumor pct: 2% in ctrl. - Total				-	2	0	0	0	1			
LUNG	(29	)	IN 92-103	1	1	0	0	0	0	0.115	0.073	0.973
X-HISTIOCYTIC SARCOMA	(321	)	IN 92-103	2	12	12	12	13	8			
			FA 77	1	0	0	0	0	1			
			FA 77	2	58	55	56	54	54			
			FA 89	1	0	0	0	1	0			
			FA 89	2	36	47	44	52	48			
			FA 105	1	0	0	0	0	1			
			FA 105	2	16	28	18	29	29			
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	1	0	0	1	2			
LUNG	(29	)	IN 79-91	1	0	0	0	0	1	0.044	0.021	0.971
B-BRONCHIOALVEOLAR ADENOM	(379	)	IN 79-91	2	21	8	12	2	10			
			IN 92-103	1	0	0	1	0	0			
			IN 92-103	2	13	12	11	13	8			
			IN 104-106	1	0	0	0	0	1			
			IN 104-106	2	21	34	29	39	32			
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	0	0	1	0	2			
LUNG	(29	)	IN 104-106	1	0	0	0	1	0	0.461	0.376	1.000
M-BRONCHIOALVEOLAR CARCIN	(406	)	IN 104-106	2	21	34	29	38	33			
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	0	0	0	1	0			
ADRENAL MEDULLA	(3	)	IN 79-91	1	1	0	0	0	1	0.945	0.935	0.997
B-PHEOCHROMOCYTOMA	(338	)	IN 79-91	2	20	8	12	2	10			
			IN 92-103	1	0	5	0	1	0			
			IN 92-103	2	13	7	12	12	8			
			IN 104-106	1	5	7	6	6	4			
			IN 104-106	2	16	27	23	33	29			
Spontaneous tumor pct: 14% in ctrl. - Total				-	6	12	6	7	5			
MAMMARY GLAND	(30	)	IN 79-91	1	1	0	0	0	0	1.000	0.869	1.000
B-FIBROMA	(169	)	IN 79-91	2	20	8	12	2	11			
			IN 92-103	1	1	0	0	0	0			
			IN 92-103	2	12	12	12	13	8			
Spontaneous tumor pct: 2% in ctrl. - Total				-	2	0	0	0	0			
MAMMARY GLAND	(30	)	IN 104-106	1	0	0	0	0	1	0.211	0.048	1.000
M-FIBROSARCOMA	(393	)	IN 104-106	2	21	34	29	39	32			
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	0	0	0	0	1			

MAMMARY GLAND	(30	)	IN 79-91	1	1	0	0	0	0	0.913	0.882	1.000
B-FIBROADENOMA	(77	)	IN 79-91	2	20	8	12	2	11			
			IN 92-103	1	0	1	0	0	0			
			IN 92-103	2	13	11	12	13	8			
			IN 104-106	1	1	0	1	1	0			
			IN 104-106	2	20	34	28	38	33			
Spontaneous tumor pct: 2%		in ctrl. -	Total	-	2	1	1	1	0			
MAMMARY GLAND	(30	)	IN 79-91	1	0	0	0	0	1	0.535	0.476	0.999
M-ADENOCARCINOMA	(96	)	IN 79-91	2	21	8	12	2	10			
			IN 92-103	1	0	1	0	0	0			
			IN 92-103	2	13	11	12	13	8			
			IN 104-106	1	0	1	0	0	0			
			IN 104-106	2	21	33	29	39	33			
Spontaneous tumor pct: 2%		in ctrl. -	Total	-	0	2	0	0	1			
MESENTERIC LYMPH	(32	)	FA 62	1	0	0	0	0	1	0.403	0.288	1.000
X-MALIGNANT LYMPHOMA	(156	)	FA 62	2	65	58	61	59	59			
			FA 84	1	1	0	0	0	0			
			FA 84	2	47	50	47	53	51			
Spontaneous tumor pct: <= 1%		in ctrl. -	Total	-	1	0	0	0	1			
MESENTERIC LYMPH	(32	)	FA 77	1	0	0	0	0	1	0.198	0.040	1.000
X-HISTIOCYTIC SARCOMA	(323	)	FA 77	2	58	55	55	54	54			
Spontaneous tumor pct: <= 1%		in ctrl. -	Total	-	0	0	0	0	1			
MESENTERIC LYMPH	(32	)	IN 92-103	1	0	1	0	0	0	1.000	0.812	1.000
X-HEMANGIOMA	(616	)	IN 92-103	2	13	11	12	13	8			
Spontaneous tumor pct: <= 1%		in ctrl. -	Total	-	0	1	0	0	0			
MULTISYSTEMIC	(34	)	FA 21	1	0	0	0	0	1	0.335	0.299	0.977
M-MALIGNANT LYMPHOMA	(118	)	FA 21	2	65	64	65	65	64			
			FA 62	1	0	0	0	0	1			
			FA 62	2	65	59	62	59	59			
			FA 70	1	0	0	0	0	1			
			FA 70	2	63	57	60	58	56			
			FA 83	1	1	0	0	0	0			
			FA 83	2	49	52	49	53	52			
			FA 84	1	1	0	0	0	0			
			FA 84	2	47	50	48	53	51			
			FA 87	1	2	0	0	0	0			
			FA 87	2	42	48	46	53	50			
Spontaneous tumor pct: 3%		in ctrl. -	Total	-	4	0	0	0	3			
MULTISYSTEMIC	(34	)	IN 92-103	1	1	0	0	0	0	0.035	0.018	0.823
M-HISTIOCYTIC SARCOMA	(134	)	IN 92-103	2	12	12	12	13	8			
			FA 55	1	0	0	0	0	1			
			FA 55	2	55	61	65	60	60			
			FA 77	1	0	0	0	0	1			
			FA 77	2	58	55	56	54	54			
			FA 89	1	0	0	0	1	0			
			FA 89	2	36	47	44	52	48			
			FA 105	1	0	0	0	0	1			
			FA 105	2	16	28	18	29	29			
Spontaneous tumor pct: <= 1%		in ctrl. -	Total	-	1	0	0	1	3			

MULTISYSTEMIC	(34	)	IN	92-103	1	0	1	0	0	0	1.000 0.812 1.000
B-HEMANGIOMA	(617	)	IN	92-103	2	13	11	12	13	8	
Spontaneous tumor pct: <= 1% in ctrl. - Total					-	0	1	0	0	0	
PANCREAS	(36	)	IN	79-91	1	2	2	0	0	0	0.929 0.913 0.999
B-ISLET CELL ADENOMA	(145	)	IN	79-91	2	19	5	12	2	11	
			IN	104-106	1	3	1	3	4	1	
			IN	104-106	2	18	33	26	35	32	
Spontaneous tumor pct: 6% in ctrl. - Total					-	5	3	3	4	1	
PANCREAS	(36	)	FA	87	1	1	0	0	0	0	1.000 0.835 1.000
X-MALIGNANT LYMPHOMA	(167	)	FA	87	2	42	47	46	53	49	
Spontaneous tumor pct: <= 1% in ctrl. - Total					-	1	0	0	0	0	
PANCREAS	(36	)	IN	53-78	1	0	0	0	1	0	0.317 0.302 1.000
B-ACINAR CELL ADENOMA	(287	)	IN	53-78	2	9	7	12	5	7	
Spontaneous tumor pct: <= 1% in ctrl. - Total					-	0	0	0	1	0	
PANCREAS	(36	)	FA	77	1	0	0	0	0	1	0.048 0.010 0.989
X-HISTIOCYTIC SARCOMA	(324	)	FA	77	2	57	54	56	54	53	
			FA	105	1	0	0	0	0	1	
			FA	105	2	16	28	18	29	29	
Spontaneous tumor pct: <= 1% in ctrl. - Total					-	0	0	0	0	2	
PANCREAS	(36	)	IN	53-78	1	0	0	1	0	0	0.715 0.691 1.000
M-ISLET CELL CARCINOMA	(347	)	IN	53-78	2	9	7	11	6	7	
			IN	104-106	1	0	0	0	1	0	
			IN	104-106	2	21	34	29	38	33	
			FA	93	1	1	0	0	0	0	
			FA	93	2	32	46	41	52	42	
Spontaneous tumor pct: <= 1% in ctrl. - Total					-	1	0	1	1	0	
PARATHYROIDS	(37	)	IN	92-103	1	0	0	0	0	1	0.487 0.452 0.992
B-ADENOMA	(496	)	IN	92-103	2	13	10	11	12	7	
			IN	104-106	1	0	1	3	2	0	
			IN	104-106	2	21	32	23	36	33	
Spontaneous tumor pct: <= 1% in ctrl. - Total					-	0	1	3	2	1	
PARATHYROIDS	(37	)	FA	105	1	0	0	0	0	1	0.258 0.069 1.000
X-HISTIOCYTIC SARCOMA	(557	)	FA	105	2	16	27	15	28	29	
Spontaneous tumor pct: <= 1% in ctrl. - Total					-	0	0	0	0	1	
PITUITARY	(38	)	FA	80	1	1	0	0	0	0	1.000 0.824 1.000
M-CARCINOMA	(100	)	FA	80	2	52	54	51	53	53	
Spontaneous tumor pct: <= 1% in ctrl. - Total					-	1	0	0	0	0	

PITUITARY	(38	) IN 53-78	1	1	0	1	0	1	1.000 1.000 1.000
B-ADENOMA	(19	) IN 53-78	2	3	6	7	2	6	
		IN 79-91	1	6	0	1	1	3	
		IN 79-91	2	9	5	7	1	8	
		IN 92-103	1	0	2	4	1	1	
		IN 92-103	2	8	3	5	9	6	
		IN 104-106	1	11	12	10	5	4	
		IN 104-106	2	10	22	19	34	29	
		FA 60	1	0	0	1	0	0	
		FA 60	2	64	60	63	59	60	
		FA 65	1	1	0	0	1	0	
		FA 65	2	62	59	62	57	59	
		FA 66	1	0	0	0	0	1	
		FA 66	2	62	59	61	57	58	
		FA 70	1	0	0	1	0	0	
		FA 70	2	62	57	59	57	57	
		FA 71	1	2	1	0	0	0	
		FA 71	2	59	56	59	57	56	
		FA 75	1	0	0	0	1	0	
		FA 75	2	58	56	58	55	55	
		FA 76	1	1	0	0	2	0	
		FA 76	2	57	56	57	53	55	
		FA 77	1	1	0	0	0	0	
		FA 77	2	56	55	56	53	55	
		FA 78	1	0	0	2	0	0	
		FA 78	2	56	55	54	53	54	
		FA 79	1	0	0	1	0	0	
		FA 79	2	55	54	52	53	54	
		FA 80	1	0	0	1	0	0	
		FA 80	2	53	54	50	53	53	
		FA 81	1	1	1	1	0	0	
		FA 81	2	51	53	49	53	53	
		FA 82	1	0	1	0	0	0	
		FA 82	2	50	52	49	52	53	
		FA 83	1	1	0	0	0	0	
		FA 83	2	48	52	49	52	52	
		FA 85	1	0	1	0	0	0	
		FA 85	2	45	49	47	52	51	
		FA 86	1	2	0	0	0	0	
		FA 86	2	43	49	47	52	51	
		FA 87	1	2	0	0	0	0	
		FA 87	2	41	48	46	52	50	
		FA 91	1	0	0	1	0	0	
		FA 91	2	35	46	41	51	47	
		FA 93	1	1	1	0	0	0	
		FA 93	2	33	45	41	51	43	
		FA 94	1	1	0	0	0	0	
		FA 94	2	30	45	41	51	43	
		FA 95	1	0	0	1	0	0	
		FA 95	2	28	45	38	50	41	
		FA 96	1	0	1	0	0	0	
		FA 96	2	28	44	37	49	39	
		FA 97	1	0	1	0	0	0	
		FA 97	2	27	42	37	49	38	
		FA 98	1	0	0	0	0	1	
		FA 98	2	26	42	37	48	37	
		FA 99	1	0	1	0	0	0	

APPEARS THIS WAY ON ORIGINAL

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			FA 99	2	26	40	34	46	36	
			FA 100	1	0	1	0	1	0	
			FA 100	2	25	38	34	44	36	
			FA 101	1	1	0	0	0	0	
			FA 101	2	23	37	33	43	35	
			FA 102	1	1	1	0	0	0	
			FA 102	2	22	36	32	42	35	
			FA 103	1	0	1	2	1	0	
			FA 103	2	22	35	30	41	35	
Spontaneous tumor pct: 45%		in ctrl. - Total		-	33	25	27	13	11	
PITUITARY	(38	)	FA 83	1	0	1	0	0	0	1.000 0.827 1.000
M-GANGLIONEUROMA	(52	)	FA 83	2	49	51	49	52	52	
Spontaneous tumor pct: <= 1%		in ctrl. - Total		-	0	1	0	0	0	
PROSTATE	(39	)	FA 62	1	0	0	0	0	1	0.607 0.545 1.000
X-MALIGNANT LYMPHOMA	(168	)	FA 62	2	65	59	62	59	59	
			FA 87	1	2	0	0	0	0	
			FA 87	2	42	48	46	53	50	
Spontaneous tumor pct: 2%		in ctrl. - Total		-	2	0	0	0	1	
PROSTATE	(39	)	FA 67	1	0	0	1	0	0	0.834 0.796 1.000
M-CARCINOMA	(238	)	FA 67	2	63	59	60	58	58	
			FA 78	1	1	0	0	0	0	
			FA 78	2	56	55	56	54	54	
Spontaneous tumor pct: <= 1%		in ctrl. - Total		-	1	0	1	0	0	
PROSTATE	(39	)	FA 77	1	0	0	0	0	1	0.197 0.039 1.000
X-HISTIOCYTIC SARCOMA	(326	)	FA 77	2	58	55	56	54	54	
Spontaneous tumor pct: <= 1%		in ctrl. - Total		-	0	0	0	0	1	
SALIVARY GLAND	(40	)	FA 62	1	0	0	0	0	1	0.197 0.039 1.000
X-MALIGNANT LYMPHOMA	(211	)	FA 62	2	65	58	62	59	59	
Spontaneous tumor pct: <= 1%		in ctrl. - Total		-	0	0	0	0	1	
SEMINAL VESICLE	(42	)	FA 77	1	0	0	0	0	1	0.218 0.048 1.000
X-HISTIOCYTIC SARCOMA	(327	)	FA 77	2	47	49	52	49	54	
Spontaneous tumor pct: <= 1%		in ctrl. - Total		-	0	0	0	0	1	
SKIN	(44	)	IN 53-78	1	0	0	0	0	1	0.226 0.176 0.998
X-HISTIOCYTIC SARCOMA	(132	)	IN 53-78	2	9	7	12	6	7	
			IN 79-91	1	0	0	0	1	0	
			IN 79-91	2	21	8	12	1	11	
			IN 92-103	1	1	0	0	0	0	
			IN 92-103	2	12	12	12	13	8	
Spontaneous tumor pct: <= 1%		in ctrl. - Total		-	1	0	0	1	1	
SKIN	(44	)	IN 79-91	1	0	0	0	1	0	0.321 0.207 1.000
M-MYXOSARCOMA	(140	)	IN 79-91	2	21	8	12	1	11	
			IN 92-103	1	0	0	0	1	0	
			IN 92-103	2	13	12	12	12	8	
Spontaneous tumor pct: <= 1%		in ctrl. - Total		-	0	0	0	2	0	
SKIN	(44	)	IN 79-91	1	0	1	0	0	0	1.000 0.763 1.000
M-NEUROFIBROSARCOMA	(204	)	IN 79-91	2	21	7	12	2	11	
Spontaneous tumor pct: <= 1%		in ctrl. - Total		-	0	1	0	0	0	

SKIN	(44	)	IN 53-78	1	1	0	0	0	0	1.000 0.999 1.000
B-FIBROMA	(268	)	IN 53-78	2	8	7	12	6	8	
			IN 79-91	1	2	0	1	0	0	
			IN 79-91	2	19	8	11	2	11	
			IN 92-103	1	1	1	0	0	0	
			IN 92-103	2	12	11	12	13	8	
			IN 104-106	1	3	6	4	1	0	
			IN 104-106	2	18	28	25	38	33	
Spontaneous tumor pct: 11% in ctrl. - Total				-	7	7	5	1	0	
SKIN	(44	)	IN 79-91	1	1	0	0	0	0	1.000 0.763 1.000
X-MALIGNANT LYMPHOMA	(277	)	IN 79-91	2	20	8	12	2	11	
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	1	0	0	0	0	
SKIN	(44	)	IN 79-91	1	0	0	1	0	0	0.174 0.139 0.997
B-KERATOACANTHOMA	(310	)	IN 79-91	2	21	8	11	2	11	
			IN 104-106	1	0	0	0	1	1	
			IN 104-106	2	21	34	29	38	32	
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	0	0	1	1	1	
SKIN	(44	)	IN 79-91	1	1	0	0	0	0	0.944 0.926 0.999
B-LIPOMA	(380	)	IN 79-91	2	20	8	12	2	11	
			IN 92-103	1	2	0	1	1	0	
			IN 92-103	2	11	12	11	12	8	
			IN 104-106	1	2	3	1	2	1	
			IN 104-106	2	19	31	28	37	32	
Spontaneous tumor pct: 6% in ctrl. - Total				-	5	3	2	3	1	
SKIN	(44	)	IN 0-52	1	0	1	0	0	0	0.914 0.882 1.000
M-FIBROSARCOMA	(41	)	IN 0-52	2	0	3	0	5	3	
			IN 79-91	1	2	0	0	0	0	
			IN 79-91	2	19	8	12	2	11	
			IN 92-103	1	0	0	0	1	0	
			IN 92-103	2	13	12	12	12	8	
			IN 104-106	1	0	1	0	1	0	
			IN 104-106	2	21	33	29	38	33	
Spontaneous tumor pct: 3% in ctrl. - Total				-	2	2	0	2	0	
SKIN	(44	)	IN 79-91	1	0	0	1	0	0	0.463 0.528 1.000
B-TRICHOEPITHELIOMA	(484	)	IN 79-91	2	21	8	11	2	11	
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	0	0	1	0	0	
SKIN	(44	)	IN 92-103	1	0	0	0	1	0	0.695 0.642 1.000
M-RHABDOMYOSARCOMA	(501	)	IN 92-103	2	13	12	12	12	8	
			IN 104-106	1	0	1	0	0	0	
			IN 104-106	2	21	33	29	39	33	
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	0	1	0	1	0	
SKIN	(44	)	IN 53-78	1	0	1	0	0	0	1.000 0.819 1.000
M-BASAL CELL CARCINOMA	(520	)	IN 53-78	2	9	6	12	6	8	
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	0	1	0	0	0	
SKIN	(44	)	IN 92-103	1	0	1	0	0	1	0.307 0.266 0.993
B-BASAL CELL TUMOR	(524	)	IN 92-103	2	13	11	12	13	7	
			IN 104-106	1	0	0	1	2	0	
			IN 104-106	2	21	34	28	37	33	
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	0	1	1	2	1	

SKIN	(44)	IN 79-91	1	0	0	0	0	1	0.507	0.461	0.999	
B-SEBACEOUS GLAND ADENOMA	(525)	IN 79-91	2	21	8	12	2	10				
		IN 104-106	1	1	0	2	0	0				
		IN 104-106	2	20	34	27	39	33				
Spontaneous tumor pct: <= 1% in ctrl.		- Total	-	1	0	2	0	1				
SKIN	(44)	IN 104-106	1	3	3	3	1	0	0.995	0.987	1.000	
B-SQUAMOUS CELL PAPILLOMA	(531)	IN 104-106	2	18	31	26	38	33				
Spontaneous tumor pct: 5% in ctrl.		- Total	-	3	3	3	1	0				
SPLEEN	(46)	FA 21	1	0	0	0	0	1	0.036	0.016	0.885	
X-MALIGNANT LYMPHOMA	(114)	FA 21	2	65	63	64	64	64				
		FA 62	1	0	0	0	0	1				
		FA 62	2	65	58	61	58	59				
		FA 70	1	0	0	0	0	1				
		FA 70	2	63	56	59	57	56				
		FA 84	1	1	0	0	0	0				
		FA 84	2	47	49	48	52	51				
Spontaneous tumor pct: <= 1% in ctrl.		- Total	-	1	0	0	0	3				
SPLEEN	(46)	IN 92-103	1	0	1	0	0	0	1.000	0.808	1.000	
M-FIBROSARCOMA	(548)	IN 92-103	2	13	11	12	12	8				
Spontaneous tumor pct: <= 1% in ctrl.		- Total	-	0	1	0	0	0				
SQUAMOUS STOMACH	(47)	FA 87	1	1	0	0	0	0	1.000	0.834	1.000	
X-MALIGNANT LYMPHOMA	(271)	FA 87	2	43	48	46	53	50				
Spontaneous tumor pct: <= 1% in ctrl.		- Total	-	1	0	0	0	0				
STOMACH	(48)	IN 92-103	1	1	0	0	0	0	1.000	0.819	1.000	
X-MALIGNANT LYMPHOMA	(389)	IN 92-103	2	10	12	12	13	8				
Spontaneous tumor pct: <= 1% in ctrl.		- Total	-	1	0	0	0	0				
TESTES	(49)	FA 55	1	0	0	0	0	1	0.195	0.038	1.000	
X-HISTIOCYTIC SARCOMA	(133)	FA 55	2	65	61	65	60	60				
Spontaneous tumor pct: <= 1% in ctrl.		- Total	-	0	0	0	0	1				
TESTES	(49)	IN 79-91	1	2	0	0	0	1	0.004	0.002	0.086	
B-INTERSTITIAL CELL ADENO	(158)	IN 79-91	2	19	8	12	2	10				
		IN 92-103	1	0	0	0	1	1				
		IN 92-103	2	13	12	12	12	7				
		IN 104-106	1	1	4	0	7	8				
		IN 104-106	2	20	30	29	32	25				
Spontaneous tumor pct: 5% in ctrl.		- Total	-	3	4	0	8	10	(Exact		P<0.005)	
TESTES	(49)	FA 87	1	1	0	0	0	0	1.000	0.834	1.000	
X-MALIGNANT LYMPHOMA	(273)	FA 87	2	43	48	46	53	50				
Spontaneous tumor pct: <= 1% in ctrl.		- Total	-	1	0	0	0	0				

THYMUS	(51	)	FA 62	1	0	0	0	0	1	0.861	0.827	1.000
X-MALIGNANT LYMPHOMA	(152	)	FA 62	2	63	55	59	56	55			
			FA 83	1	1	0	0	0	0			
			FA 83	2	47	49	46	50	50			
			FA 84	1	1	0	0	0	0			
			FA 84	2	45	47	45	50	49			
			FA 87	1	2	0	0	0	0			
			FA 87	2	40	45	43	50	48			
Spontaneous tumor pct: 3%	in ctrl. - Total			-	4	0	0	0	1			
THYMUS	(51	)	FA 72	1	0	0	0	1	0	0.671	0.639	1.000
M-THYMOMA	(193	)	FA 72	2	57	53	56	54	53			
			FA 76	1	0	1	0	0	0			
			FA 76	2	57	52	54	53	52			
Spontaneous tumor pct: <= 1%	in ctrl. - Total			-	0	1	0	1	0			
THYMUS	(51	)	FA 89	1	0	0	0	1	0	0.446	0.372	1.000
X-HISTIOCYTIC SARCOMA	(384	)	FA 89	2	34	44	41	49	46			
Spontaneous tumor pct: <= 1%	in ctrl. - Total			-	0	0	0	1	0			
THYROIDS	(52	)	IN 79-91	1	1	1	0	0	0	0.898	0.863	1.000
B-FOLLICULAR CELL ADENOMA	(157	)	IN 79-91	2	20	6	11	2	11			
			IN 104-106	1	0	1	0	1	0			
			IN 104-106	2	21	33	29	38	33			
Spontaneous tumor pct: 2%	in ctrl. - Total			-	1	2	0	1	0			
THYROIDS	(52	)	IN 53-78	1	1	0	0	0	0	0.819	0.802	0.989
B-C-CELL ADENOMA	(248	)	IN 53-78	2	8	7	10	6	5			
			IN 79-91	1	1	0	0	0	0			
			IN 79-91	2	20	7	11	2	11			
			IN 92-103	1	2	2	1	2	0			
			IN 92-103	2	9	8	10	11	8			
			IN 104-106	1	4	3	1	4	4			
			IN 104-106	2	17	31	28	35	29			
Spontaneous tumor pct: 10%	in ctrl. - Total			-	8	5	2	6	4			
THYROIDS	(52	)	IN 92-103	1	1	0	0	0	1	0.393	0.351	0.992
M-FOLLICULAR CELL CARCINO	(289	)	IN 92-103	2	10	10	11	12	7			
			IN 104-106	1	0	1	0	0	1			
			IN 104-106	2	21	33	29	39	32			
			FA 87	1	1	0	0	0	0			
			FA 87	2	41	45	45	53	50			
			FA 95	1	0	0	0	1	0			
			FA 95	2	27	44	38	50	41			
Spontaneous tumor pct: 2%	in ctrl. - Total			-	2	1	0	1	2			
URINARY BLADDER	(56	)	FA 87	1	1	0	0	0	0	1.000	0.836	1.000
X-MALIGNANT LYMPHOMA	(275	)	FA 87	2	42	46	45	52	50			
Spontaneous tumor pct: <= 1%	in ctrl. - Total			-	1	0	0	0	0			
URINARY BLADDER	(56	)	FA 89	1	0	0	0	1	0	0.448	0.374	1.000
X-HISTIOCYTIC SARCOMA	(427	)	FA 89	2	35	45	43	51	48			
Spontaneous tumor pct: <= 1%	in ctrl. - Total			-	0	0	0	1	0			

BONE MARROW	(7	)	FA 21	1	0	0	0	0	1	0.205	0.167	0.961
X-MALIGNANT LYMPHOMA	(116	)	FA 21	2	65	64	65	65	64			
			FA 62	1	0	0	0	0	1			
			FA 62	2	65	59	62	59	59			
			FA 70	1	0	0	0	0	1			
			FA 70	2	63	57	60	58	56			
			FA 83	1	1	0	0	0	0			
			FA 83	2	49	52	49	53	52			
			FA 84	1	1	0	0	0	0			
			FA 84	2	47	50	48	53	51			
			FA 87	1	1	0	0	0	0			
			FA 87	2	43	48	46	53	50			
Spontaneous tumor pct: 2%		in ctrl. -	Total	-	3	0	0	0	3			
BONE MARROW	(7	)	FA 77	1	0	0	0	0	1	0.197	0.039	1.000
X-HISTIOCYTIC SARCOMA	(328	)	FA 77	2	58	55	56	54	54			
Spontaneous tumor pct: <= 1%		in ctrl. -	Total	-	0	0	0	0	1			
BRAIN	(9	)	FA 62	1	0	0	0	0	1	0.600	0.539	1.000
X-MALIGNANT LYMPHOMA	(153	)	FA 62	2	65	59	62	59	59			
			FA 83	1	1	0	0	0	0			
			FA 83	2	49	52	49	53	52			
			FA 87	1	1	0	0	0	0			
			FA 87	2	43	48	46	53	50			
Spontaneous tumor pct: 2%		in ctrl. -	Total	-	2	0	0	0	1			
BRAIN	(9	)	IN 104-106	1	0	2	0	2	1	0.487	0.455	0.983
M-ASTROCYTOMA	(48	)	IN 104-106	2	21	32	29	37	32			
			FA 43	1	0	1	0	0	0			
			FA 43	2	65	62	65	63	63			
			FA 81	1	0	0	0	1	0			
			FA 81	2	53	54	50	53	53			
			FA 88	1	0	0	0	0	1			
			FA 88	2	36	47	44	53	49			
			FA 103	1	0	1	0	0	0			
			FA 103	2	22	35	32	42	35			
Spontaneous tumor pct: 3%		in ctrl. -	Total	-	0	4	0	3	2			
BRAIN	(9	)	IN 104-106	1	0	0	0	0	1	0.211	0.048	1.000
B-LIPOMA	(573	)	IN 104-106	2	21	34	29	39	32			
Spontaneous tumor pct: <= 1%		in ctrl. -	Total	-	0	0	0	0	1			
BRAIN	(9	)	FA 86	1	0	0	0	0	1	0.207	0.045	1.000
M-UNDIFFERENTIATED GLIOMA	(624	)	FA 86	2	46	49	47	53	50			
Spontaneous tumor pct: <= 1%		in ctrl. -	Total	-	0	0	0	0	1			

APPEARS THIS WAY
ON ORIGINAL

Appendix 2: Analysis of Carcinogenic Potential in Female Rat
Test of Dose-Response (Tumor) Positive Linear Trend
Study No.
Run Date & Time: June 4, 1999 (15:56)
Source: C:\NDAS\RAPCARC\RAT103\st95103.lis

Note: Dose Levels Included: CTRL1 CTRL2 LOW MED HIGH (0 0 0.05 0.1 0.2)
Missing value in Tumor-Caused Death is treated as tumor not causing death
Tumor Type: IN: Incidental (nonfatal) tumor, FA: Fatal tumor.

ORGAN/TISSUE NAME / AND TUMOR NAME	(ORG#) / (TMR#)	TUMOR TYPES	TIME STRATA	ROW NO.	2xC CONTINGENCY -------TABLES-------	EXACT PROB	ASYMP PROB	ASYMP PROB /CONT CORR =P(STAT .GE. OBSERVED)
CERVICAL LYMPH	(12	) FA	96	1	0 1 0 0 0	1.000	0.832	1.000
X-HISTIOCYTIC SARCOMA	(335	) FA	96	2	28 29 35 32 30			
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	0 1 0 0 0			
CERVIX	(13	) IN	53-78	1	0 0 0 1 0	0.125	0.094	0.927
B-FIBROMA	(291	) IN	53-78	2	15 13 11 11 10			
		IN	79-91	1	0 0 0 1 0			
		IN	79-91	2	16 15 10 12 16			
		IN	92-103	1	0 0 0 2 0			
		IN	92-103	2	19 14 28 13 15			
		IN	104-106	1	0 0 1 0 1			
		IN	104-106	2	15 20 14 21 19			
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	0 0 1 4 1			
CERVIX	(13	) FA	80	1	0 0 0 0 1	0.390	0.281	1.000
X-HISTIOCYTIC SARCOMA	(340	) FA	80	2	50 48 53 48 48			
		FA	92	1	0 1 0 0 0			
		FA	92	2	34 33 43 36 35			
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	0 1 0 0 1			
CERVIX	(13	) IN	92-103	1	1 0 1 0 0	0.693	0.671	1.000
M-STROMAL SARCOMA	(468	) IN	92-103	2	18 14 27 15 15			
		IN	104-106	1	0 0 0 1 0			
		IN	104-106	2	15 20 15 20 20			
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	1 0 1 1 0			
CERVIX	(13	) IN	92-103	1	0 0 1 0 0	0.637	0.584	1.000
M-GRANULAR CELL TUMOR	(628	) IN	92-103	2	19 14 27 15 15			
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	0 0 1 0 0			
COLON	(15	) FA	89	1	0 0 0 0 1	0.176	0.031	1.000
M-SCHWANNOMA	(473	) FA	89	2	42 35 45 37 33			
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	0 0 0 0 1			
DUODENUM	(16	) FA	78	1	0 1 0 0 0	1.000	0.824	1.000
M-LEIOMYOSARCOMA	(293	) FA	78	2	51 48 52 48 51			
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	0 1 0 0 0			
DUODENUM	(16	) FA	96	1	0 1 0 0 0	1.000	0.827	1.000
X-HISTIOCYTIC SARCOMA	(386	) FA	96	2	29 29 36 31 28			
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	0 1 0 0 0			

ADRENAL CORTEX	(2)	IN	79-91	1	0	1	0	1	0	0.814	0.787	0.999
B-CORTICAL ADENOMA	(264)	IN	79-91	2	16	14	10	12	16			
		IN	92-103	1	0	1	0	0	0			
		IN	92-103	2	19	13	28	15	15			
		IN	104-106	1	1	0	1	2	0			
		IN	104-106	2	14	20	14	19	20			
Spontaneous tumor pct: 2% in ctrl. - Total				-	1	2	1	3	0			
ADRENAL CORTEX	(2)	IN	104-106	1	0	0	0	1	0	0.450	0.373	1.000
M-CORTICAL CARCINOMA	(570)	IN	104-106	2	15	20	15	20	20			
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	0	0	0	1	0			
HEART	(22)	FA	92	1	0	1	0	0	0	1.000	0.830	1.000
X-HISTIOCYTIC SARCOMA	(443)	FA	92	2	34	33	43	36	35			
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	0	1	0	0	0			
HEART	(22)	IN	79-91	1	2	0	0	0	0	0.791	0.759	0.999
M-ENDOCARDIAL SCHWANNOMA	(447)	IN	79-91	2	14	15	10	13	16			
		IN	92-103	1	0	1	0	0	0			
		IN	92-103	2	19	13	28	15	15			
		IN	104-106	1	1	0	0	1	0			
		IN	104-106	2	14	20	15	20	19			
		FA	105	1	0	0	0	0	1			
		FA	105	2	15	20	15	21	19			
Spontaneous tumor pct: 3% in ctrl. - Total				-	3	1	0	1	1			
JEJUNUM	(24)	IN	92-103	1	0	1	0	0	0	1.000	0.819	1.000
M-LEIOMYOSARCOMA	(521)	IN	92-103	2	18	11	27	13	11			
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	0	1	0	0	0			
KIDNEYS	(25)	FA	68	1	1	0	0	0	0	1.000	0.822	1.000
M-LIPOSARCOMA	(35)	FA	68	2	59	57	57	56	57			
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	1	0	0	0	0			
KIDNEYS	(25)	FA	96	1	0	1	0	0	0	1.000	0.912	1.000
X-HISTIOCYTIC SARCOMA	(382)	FA	96	2	29	30	36	32	30			
		FA	104	1	0	1	0	0	0			
		FA	104	2	20	24	27	24	24			
Spontaneous tumor pct: 2% in ctrl. - Total				-	0	2	0	0	0			
KIDNEYS	(25)	IN	79-91	1	1	0	0	0	0	1.000	0.816	1.000
B-TUBULAR CELL ADENOMA	(401)	IN	79-91	2	15	15	10	13	16			
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	1	0	0	0	0			
KIDNEYS	(25)	FA	89	1	0	0	1	0	0	0.605	0.597	1.000
M-RENAL MESENCHYMAL TUMOR	(485)	FA	89	2	43	39	46	40	39			
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	0	0	1	0	0			
KIDNEYS	(25)	IN	104-106	1	0	0	0	0	1	0.219	0.051	1.000
B-LIPOMA	(581)	IN	104-106	2	15	20	15	21	19			
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	0	0	0	0	1			
LIVER	(26)	IN	104-106	1	1	0	0	1	0	0.726	0.680	1.000
B-HEPATOCELLULAR ADENOMA	(159)	IN	104-106	2	14	20	15	20	20			
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	1	0	0	1	0			

LIVER	(26	) FA 75	1	1	0	0	0	0	1.000 0.826 1.000
M-HEPATOCELLULAR CARCINOM	(218	) FA 75	2	53	53	54	54	54	
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	1	0	0	0	0	
LIVER	(26	) IN 104-106	1	1	0	0	0	0	0.621 0.592 0.997
X-HISTIOCYTIC SARCOMA	(322	) IN 104-106	2	14	20	15	21	20	
		FA 70	1	0	0	1	0	0	
		FA 70	2	57	57	56	56	57	
		FA 79	1	0	0	0	0	1	
		FA 79	2	50	49	53	49	50	
		FA 80	1	0	0	0	0	1	
		FA 80	2	50	48	53	48	48	
		FA 92	1	0	1	0	0	0	
		FA 92	2	34	33	43	36	35	
		FA 96	1	0	1	0	0	0	
		FA 96	2	29	30	36	32	30	
		FA 104	1	0	1	0	0	0	
		FA 104	2	20	24	27	24	24	
Spontaneous tumor pct: 3% in ctrl. - Total			-	1	3	1	0	2	
LUNG	(29	) FA 79	1	0	0	0	0	1	0.263 0.211 0.994
X-HISTIOCYTIC SARCOMA	(321	) FA 79	2	50	49	53	49	50	
		FA 80	1	0	0	0	0	1	
		FA 80	2	50	48	53	48	48	
		FA 92	1	0	1	0	0	0	
		FA 92	2	34	33	43	36	35	
		FA 104	1	0	1	0	0	0	
		FA 104	2	20	24	27	24	24	
Spontaneous tumor pct: 2% in ctrl. - Total			-	0	2	0	0	2	
LUNG	(29	) IN 79-91	1	1	0	0	0	0	1.000 0.816 1.000
B-BRONCHIOALVEOLAR ADENOM	(379	) IN 79-91	2	15	15	10	13	16	
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	1	0	0	0	0	
LUNG	(29	) IN 79-91	1	1	0	0	0	0	1.000 0.816 1.000
M-BRONCHIOALVEOLAR CARCIN	(406	) IN 79-91	2	15	15	10	13	16	
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	1	0	0	0	0	
LUNG	(29	) IN 92-103	1	0	1	0	0	0	1.000 0.825 1.000
M-MESOTHELIOMA	(620	) IN 92-103	2	19	13	28	15	15	
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	0	1	0	0	0	
ADRENAL MEDULLA	(3	) IN 79-91	1	0	0	0	0	1	0.633 0.596 0.999
B-PHEOCHROMOCYTOMA	(338	) IN 79-91	2	16	15	10	13	15	
		IN 92-103	1	0	1	0	0	0	
		IN 92-103	2	19	13	28	15	15	
		IN 104-106	1	1	0	1	0	0	
		IN 104-106	2	14	20	14	21	20	
Spontaneous tumor pct: 2% in ctrl. - Total			-	1	1	1	0	1	

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MAMMARY GLAND	(30)	IN 53-78	1	1	0	0	0	0	0.992 0.983 1.000
B-FIBROMA	(169)	IN 53-78	2	14	13	11	12	10	
		IN 79-91	1	1	1	1	0	0	
		IN 79-91	2	15	14	9	13	16	
		IN 92-103	1	0	1	2	0	0	
		IN 92-103	2	19	13	26	15	15	
		IN 104-106	1	0	3	1	1	0	
		IN 104-106	2	15	17	14	20	20	
Spontaneous tumor pct: 5%	in ctrl. -	Total	-	2	5	4	1	0	
MAMMARY GLAND	(30)	IN 53-78	1	1	0	0	0	0	0.754 0.708 0.999
B-LIPOMA	(187)	IN 53-78	2	14	13	11	12	10	
		IN 79-91	1	0	0	0	0	1	
		IN 79-91	2	16	15	10	13	15	
		IN 104-106	1	0	2	0	0	0	
		IN 104-106	2	15	18	15	21	20	
Spontaneous tumor pct: 2%	in ctrl. -	Total	-	1	2	0	0	1	
MAMMARY GLAND	(30)	IN 79-91	1	1	0	0	0	0	1.000 0.908 1.000
M-FIBROSARCOMA	(393)	IN 79-91	2	15	15	10	13	16	
		IN 104-106	1	0	1	0	0	0	
		IN 104-106	2	15	19	15	21	20	
Spontaneous tumor pct: 2%	in ctrl. -	Total	-	1	1	0	0	0	
MAMMARY GLAND	(30)	IN 79-91	1	1	0	0	0	0	1.000 0.816 1.000
B-ADENOLIPOMA	(404)	IN 79-91	2	15	15	10	13	16	
Spontaneous tumor pct: <= 1%	in ctrl. -	Total	-	1	0	0	0	0	
MAMMARY GLAND	(30)	IN 79-91	1	0	1	0	0	0	0.839 0.793 1.000
M-NEUROFIBROSARCOMA	(491)	IN 79-91	2	16	14	10	13	16	
		IN 92-103	1	0	0	1	0	0	
		IN 92-103	2	19	14	27	15	15	
Spontaneous tumor pct: <= 1%	in ctrl. -	Total	-	0	1	1	0	0	
MAMMARY GLAND	(30)	IN 0-52	1	0	0	1	2	0	0.999 0.999 1.000
B-FIBROADENOMA	(77)	IN 0-52	2	0	3	0	2	4	
		IN 53-78	1	6	4	3	3	3	
		IN 53-78	2	9	9	8	9	7	
		IN 79-91	1	12	8	4	4	3	
		IN 79-91	2	4	7	6	9	13	
		IN 92-103	1	14	10	20	7	8	
		IN 92-103	2	5	4	8	8	7	
		IN 104-106	1	9	11	6	15	7	
		IN 104-106	2	6	9	9	6	13	
Spontaneous tumor pct: 57%	in ctrl. -	Total	-	41	33	34	31	21	
MAMMARY GLAND	(30)	IN 0-52	1	0	0	0	2	1	0.981 0.978 0.998
M-ADENOCARCINOMA	(96)	IN 0-52	2	0	3	1	2	3	
		IN 53-78	1	4	6	4	3	1	
		IN 53-78	2	11	7	7	9	9	
		IN 79-91	1	8	3	1	2	2	
		IN 79-91	2	8	12	9	11	14	
		IN 92-103	1	4	3	7	3	2	
		IN 92-103	2	15	11	21	12	13	
		IN 104-106	1	5	4	3	4	4	
		IN 104-106	2	10	16	12	17	16	
Spontaneous tumor pct: 28%	in ctrl. -	Total	-	21	16	15	14	10	

MAMMARY GLAND	(30)	IN 0-52	1	0	0	0	0	1	0.658	0.643	0.918
B-ADENOMA	(98)	IN 0-52	2	0	3	1	4	3			
		IN 53-78	1	0	2	2	2	0			
		IN 53-78	2	15	11	9	10	10			
		IN 79-91	1	4	6	4	2	1			
		IN 79-91	2	12	9	6	11	15			
		IN 92-103	1	2	2	3	1	3			
		IN 92-103	2	17	12	25	14	12			
		IN 104-106	1	2	4	2	1	6			
		IN 104-106	2	13	16	13	20	14			
Spontaneous tumor pct: 17% in ctrl. - Total			-	8	14	11	6	11			
MESENTERIC LYMPH	(32)	FA 92	1	0	1	0	0	0	1.000	0.910	1.000
X-HISTIOCYTIC SARCOMA	(323)	FA 92	2	34	33	43	36	34			
		FA 96	1	0	1	0	0	0			
		FA 96	2	29	30	36	32	29			
Spontaneous tumor pct: 2% in ctrl. - Total			-	0	2	0	0	0			
MULTISYSTEMIC	(34)	IN 104-106	1	0	0	0	0	1	0.219	0.051	1.000
M-MALIGNANT LYMPHOMA	(118)	IN 104-106	2	15	20	15	21	19			
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	0	0	0	0	1			
MULTISYSTEMIC	(34)	IN 104-106	1	1	0	0	0	0	0.621	0.592	0.997
M-HISTIOCYTIC SARCOMA	(134)	IN 104-106	2	14	20	15	21	20			
		FA 70	1	0	0	1	0	0			
		FA 70	2	57	57	56	56	57			
		FA 79	1	0	0	0	0	1			
		FA 79	2	50	49	53	49	50			
		FA 80	1	0	0	0	0	1			
		FA 80	2	50	48	53	48	48			
		FA 92	1	0	1	0	0	0			
		FA 92	2	34	33	43	36	35			
		FA 96	1	0	1	0	0	0			
		FA 96	2	29	30	36	32	30			
		FA 104	1	0	1	0	0	0			
		FA 104	2	20	24	27	24	24			
Spontaneous tumor pct: 3% in ctrl. - Total			-	1	3	1	0	2			
OVARIES	(35)	IN 79-91	1	0	0	0	1	0	0.467	0.448	1.000
B-THECOMA	(392)	IN 79-91	2	16	15	10	12	16			
		IN 92-103	1	0	0	1	0	0			
		IN 92-103	2	19	14	27	15	15			
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	0	0	1	1	0			
PANCREAS	(36)	IN 92-103	1	1	0	2	0	0	0.970	0.937	1.000
B-ISLET CELL ADENOMA	(145)	IN 92-103	2	18	14	26	15	15			
		IN 104-106	1	1	1	0	0	0			
		IN 104-106	2	14	19	15	21	20			
Spontaneous tumor pct: 2% in ctrl. - Total			-	2	1	2	0	0			
PANCREAS	(36)	IN 79-91	1	0	0	0	1	0	0.467	0.448	1.000
B-ACINAR CELL ADENOMA	(287)	IN 79-91	2	16	15	10	12	16			
		IN 92-103	1	0	0	1	0	0			
		IN 92-103	2	19	14	27	15	15			
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	0	0	1	1	0			

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PANCREAS	(36	) FA 92	1	0	1	0	0	0	1.000 0.911 1.000
X-HISTIOCYTIC SARCOMA	(324	) FA 92	2	34	33	43	36	35	
		FA 96	1	0	1	0	0	0	
		FA 96	2	29	30	36	32	30	
Spontaneous tumor pct: 2%		in ctrl. - Total	-	0	2	0	0	0	
PANCREAS	(36	) IN 79-91	1	1	0	0	0	0	1.000 0.816 1.000
M-ISLET CELL CARCINOMA	(347	) IN 79-91	2	15	15	10	13	16	
Spontaneous tumor pct: <= 1%		in ctrl. - Total	-	1	0	0	0	0	
PARATHYROIDS	(37	) IN 92-103	1	1	0	1	0	0	0.955 0.927 1.000
B-ADENOMA	(496	) IN 92-103	2	17	14	26	12	12	
		IN 104-106	1	1	2	0	1	0	
		IN 104-106	2	14	18	13	18	18	
Spontaneous tumor pct: 3%		in ctrl. - Total	-	2	2	1	1	0	
PITUITARY	(38	) IN 92-103	1	0	1	0	0	0	0.206 0.179 0.868
M-CARCINOMA	(100	) IN 92-103	2	19	13	26	14	15	
		IN 104-106	1	0	0	0	1	2	
		IN 104-106	2	15	20	15	20	18	
		FA 60	1	0	0	0	1	0	
		FA 60	2	63	60	60	58	59	
		FA 80	1	0	1	0	0	0	
		FA 80	2	50	47	53	48	48	
		FA 81	1	0	1	0	0	0	
		FA 81	2	50	46	53	46	45	
		FA 89	1	0	0	0	0	1	
		FA 89	2	43	39	47	40	38	
		FA 98	1	0	0	1	0	0	
		FA 98	2	28	27	33	31	28	
		FA 100	1	0	0	1	0	0	
		FA 100	2	26	27	29	28	26	
		FA 104	1	0	0	0	1	0	
		FA 104	2	20	25	27	23	24	
Spontaneous tumor pct: 2%		in ctrl. - Total	-	0	3	2	3	3	
PITUITARY	(38	) IN 0-52	1	0	0	0	1	0	0.539 0.532 0.724
B-ADENOMA	(19	) IN 0-52	2	0	1	1	2	2	
		IN 53-78	1	3	2	2	4	1	
		IN 53-78	2	3	2	1	2	3	
		IN 79-91	1	6	2	0	0	4	
		IN 79-91	2	1	3	1	1	3	
		IN 92-103	1	7	4	13	1	5	
		IN 92-103	2	4	6	6	5	3	
		IN 104-106	1	10	13	10	13	15	
		IN 104-106	2	5	7	5	8	5	
		FA 38	1	0	1	0	0	0	
		FA 38	2	64	63	65	63	64	
		FA 43	1	0	0	0	0	1	
		FA 43	2	64	63	65	63	63	
		FA 47	1	0	1	0	0	0	
		FA 47	2	64	62	65	63	62	
		FA 49	1	0	0	0	0	1	
		FA 49	2	64	62	65	63	61	
		FA 51	1	0	0	0	1	0	
		FA 51	2	64	62	65	61	61	
		FA 53	1	0	0	1	0	0	

FA 53	2	64	62	63	61	60
FA 55	1	0	1	1	0	0
FA 55	2	63	61	62	61	60
FA 57	1	0	0	1	0	1
FA 57	2	63	61	61	60	59
FA 58	1	0	1	0	0	0
FA 58	2	63	60	61	60	59
FA 59	1	0	0	1	1	0
FA 59	2	63	60	60	59	59
FA 60	1	1	1	0	0	0
FA 60	2	62	59	60	59	59
FA 61	1	1	0	0	0	0
FA 61	2	61	59	59	58	59
FA 63	1	0	1	1	0	0
FA 63	2	61	57	57	58	57
FA 65	1	0	0	0	1	0
FA 65	2	61	57	57	57	57
FA 67	1	0	0	0	1	0
FA 67	2	59	57	57	56	57
FA 69	1	1	0	0	0	0
FA 69	2	58	57	57	56	56
FA 70	1	1	0	0	0	1
FA 70	2	56	57	57	56	55
FA 71	1	0	1	0	0	0
FA 71	2	55	56	56	56	55
FA 72	1	0	1	0	1	2
FA 72	2	55	54	56	55	53
FA 73	1	1	0	1	0	0
FA 73	2	54	54	55	55	53
FA 74	1	0	0	1	0	0
FA 74	2	54	54	54	55	53
FA 75	1	0	2	0	0	0
FA 75	2	54	51	54	54	53
FA 76	1	2	0	0	0	0
FA 76	2	51	51	54	53	53
FA 77	1	0	1	1	1	0
FA 77	2	51	50	53	50	53
FA 78	1	1	0	0	1	2
FA 78	2	50	50	53	49	51
FA 79	1	0	0	0	1	1
FA 79	2	50	49	53	48	49
FA 80	1	0	0	0	2	2
FA 80	2	50	48	53	46	46
FA 81	1	0	0	0	0	1
FA 81	2	50	47	53	46	44
FA 82	1	0	3	1	2	1
FA 82	2	49	43	52	44	42
FA 83	1	1	0	1	1	0
FA 83	2	48	43	51	43	42
FA 84	1	0	3	0	0	0
FA 84	2	46	40	51	42	42
FA 85	1	0	0	1	0	1
FA 85	2	46	40	50	42	41
FA 86	1	0	0	2	2	0
FA 86	2	46	40	48	40	41
FA 88	1	1	1	1	0	0
FA 88	2	44	39	47	40	39

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			FA 89	1	3	1	1	1	1	
			FA 89	2	40	38	46	39	38	
			FA 90	1	3	1	1	1	1	
			FA 90	2	36	36	44	38	35	
			FA 91	1	1	1	1	2	0	
			FA 91	2	34	34	43	36	35	
			FA 92	1	1	0	2	1	0	
			FA 92	2	33	34	41	35	35	
			FA 93	1	1	1	0	0	1	
			FA 93	2	32	31	41	35	34	
			FA 94	1	1	0	2	1	2	
			FA 94	2	31	31	39	34	32	
			FA 95	1	2	0	2	1	0	
			FA 95	2	29	31	37	32	31	
			FA 96	1	0	1	1	0	1	
			FA 96	2	29	30	35	32	29	
			FA 97	1	0	1	1	0	1	
			FA 97	2	28	27	34	32	28	
			FA 98	1	0	0	1	2	1	
			FA 98	2	28	27	33	29	27	
			FA 99	1	0	0	0	1	0	
			FA 99	2	27	27	32	28	26	
			FA 100	1	2	0	0	1	1	
			FA 100	2	24	27	30	27	25	
			FA 102	1	1	1	0	2	0	
			FA 102	2	21	26	28	25	24	
Spontaneous tumor pct: 75% in ctrl. - Total				-	51	46	51	47	48	
PITUITARY	(38	)	FA 36	1	0	1	0	0	0	1.000 0.824 1.000
M-GANGLIONEUROMA	(52	)	FA 36	2	64	64	65	63	64	
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	0	1	0	0	0	
SALIVARY GLAND	(40	)	IN 104-106	1	0	0	0	0	1	0.219 0.051 1.000
X-MALIGNANT LYMPHOMA	(211	)	IN 104-106	2	15	20	15	21	19	
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	0	0	0	0	1	
SALIVARY GLAND	(40	)	FA 96	1	0	1	0	0	0	1.000 0.829 1.000
X-HISTIOCYTIC SARCOMA	(387	)	FA 96	2	29	30	36	32	30	
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	0	1	0	0	0	
SCIATIC NERVE	(41	)	FA 80	1	0	0	0	0	1	0.396 0.286 1.000
X-HISTIOCYTIC SARCOMA	(336	)	FA 80	2	50	48	53	48	48	
			FA 104	1	0	1	0	0	0	
			FA 104	2	20	24	27	24	24	
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	0	1	0	0	1	
SKELETAL MUSCLE	(43	)	IN 79-91	1	0	0	0	0	1	0.556 0.503 1.000
X-HISTIOCYTIC SARCOMA	(337	)	IN 79-91	2	16	15	10	13	15	
			IN 92-103	1	0	2	0	0	0	
			IN 92-103	2	19	12	28	15	15	
Spontaneous tumor pct: 2% in ctrl. - Total				-	0	2	0	0	1	

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SKIN	(44	)	IN 53-78	1	0	0	1	0	0	0.390	0.341	0.999
X-HISTIOCYTIC SARCOMA	(132	)	IN 53-78	2	15	13	10	12	10			
			IN 79-91	1	0	0	0	0	1			
			IN 79-91	2	16	15	10	13	15			
			IN 92-103	1	0	1	0	0	0			
			IN 92-103	2	19	13	28	15	15			
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	0	1	1	0	1			
SKIN	(44	)	IN 0-52	1	0	0	0	0	1	0.333	0.108	1.000
M-MYXOSARCOMA	(140	)	IN 0-52	2	0	3	1	4	3			
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	0	0	0	0	1			
SKIN	(44	)	IN 92-103	1	0	0	0	1	0	0.329	0.306	1.000
B-KERATOACANTHOMA	(310	)	IN 92-103	2	19	14	28	14	15			
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	0	0	0	1	0			
SKIN	(44	)	IN 104-106	1	0	0	1	0	0	0.615	0.629	1.000
B-LIPOMA	(380	)	IN 104-106	2	15	20	14	21	20			
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	0	0	1	0	0			
SKIN	(44	)	IN 53-78	1	0	0	0	0	1	0.163	0.027	1.000
M-FIBROSARCOMA	(41	)	IN 53-78	2	15	13	11	12	9			
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	0	0	0	0	1			
SPLEEN	(46	)	FA 96	1	0	1	0	0	0	1.000	0.829	1.000
X-HISTIOCYTIC SARCOMA	(383	)	FA 96	2	29	30	36	32	30			
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	0	1	0	0	0			
SPLEEN	(46	)	IN 104-106	1	0	0	0	0	1	0.219	0.051	1.000
M-UNDIFFERENTIATED SARCOM	(607	)	IN 104-106	2	15	20	15	21	19			
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	0	0	0	0	1			
STOMACH	(48	)	FA 96	1	0	1	0	0	0	1.000	0.829	1.000
X-HISTIOCYTIC SARCOMA	(385	)	FA 96	2	29	30	36	32	30			
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	0	1	0	0	0			
STOMACH	(48	)	FA 94	1	0	0	0	1	0	0.398	0.348	1.000
M-UNDIFFERENTIATED SARCOM	(429	)	FA 94	2	32	31	41	34	34			
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	0	0	0	1	0			
THYMUS	(51	)	FA 32	1	0	0	0	1	0	0.394	0.340	1.000
M-MESOTHELIOMA	(105	)	FA 32	2	63	62	62	60	61			
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	0	0	0	1	0			
THYMUS	(51	)	IN 104-106	1	0	1	0	0	0	1.000	0.840	1.000
M-THYMOMA	(193	)	IN 104-106	2	14	18	15	20	20			
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	0	1	0	0	0			
THYMUS	(51	)	FA 96	1	0	1	0	0	0	1.000	0.828	1.000
X-HISTIOCYTIC SARCOMA	(384	)	FA 96	2	28	29	35	31	28			
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	0	1	0	0	0			
THYROIDS	(52	)	IN 104-106	1	0	2	0	2	0	0.792	0.749	1.000
B-FOLLICULAR CELL ADENOMA	(157	)	IN 104-106	2	15	18	15	19	20			
Spontaneous tumor pct: 2% in ctrl. - Total				-	0	2	0	2	0			

THYROIDS	(52	)	IN 79-91	1	1	0	0	1	0	0.949 0.936 0.999
B-C-CELL ADENOMA	(248	)	IN 79-91	2	15	15	10	12	16	
			IN 92-103	1	2	2	0	2	0	
			IN 92-103	2	17	12	28	13	15	
			IN 104-106	1	1	3	5	2	1	
			IN 104-106	2	14	17	10	19	19	
Spontaneous tumor pct: 7%	in ctrl. -		Total	-	4	5	5	5	1	
THYROIDS	(52	)	IN 79-91	1	0	0	1	1	0	0.493 0.474 1.000
M-FOLLICULAR CELL CARCINO	(289	)	IN 79-91	2	16	15	9	12	16	
Spontaneous tumor pct: <= 1%	in ctrl. -		Total	-	0	0	1	1	0	
THYROIDS	(52	)	IN 92-103	1	1	0	0	0	0	0.386 0.280 1.000
M-C-CELL CARCINOMA	(405	)	IN 92-103	2	18	14	28	15	15	
			IN 104-106	1	0	0	0	0	1	
			IN 104-106	2	15	20	15	21	19	
Spontaneous tumor pct: <= 1%	in ctrl. -		Total	-	1	0	0	0	1	
THYROIDS	(52	)	IN 79-91	1	0	1	0	0	0	1.000 0.816 1.000
M-UNDIFFERENTIATED CARCIN	(493	)	IN 79-91	2	16	14	10	13	16	
Spontaneous tumor pct: <= 1%	in ctrl. -		Total	-	0	1	0	0	0	
VAGINA	(58	)	IN 92-103	1	0	1	0	0	0	0.216 0.172 0.982
M-STROMAL SARCOMA	(179	)	IN 92-103	2	19	13	28	15	15	
			IN 104-106	1	0	0	0	0	1	
			IN 104-106	2	15	20	15	21	19	
			FA 69	1	1	0	0	0	0	
			FA 69	2	58	57	57	56	57	
			FA 83	1	0	0	0	1	0	
			FA 83	2	49	43	52	43	43	
			FA 86	1	0	0	0	0	1	
			FA 86	2	46	40	50	42	40	
Spontaneous tumor pct: 2%	in ctrl. -		Total	-	1	1	0	1	2	
VAGINA	(58	)	IN 53-78	1	0	1	1	0	0	0.821 0.780 1.000
B-FIBROMA	(234	)	IN 53-78	2	15	12	10	12	10	
			IN 104-106	1	0	0	1	0	0	
			IN 104-106	2	15	20	14	21	20	
Spontaneous tumor pct: <= 1%	in ctrl. -		Total	-	0	1	2	0	0	
VAGINA	(58	)	FA 80	1	0	0	0	0	1	0.390 0.281 1.000
X-HISTIOCYTIC SARCOMA	(339	)	FA 80	2	50	48	53	48	48	
			FA 92	1	0	1	0	0	0	
			FA 92	2	34	33	43	36	35	
Spontaneous tumor pct: <= 1%	in ctrl. -		Total	-	0	1	0	0	1	
VAGINA	(58	)	IN 92-103	1	1	0	0	0	0	1.000 0.825 1.000
M-SQUAMOUS CELL CARCINOMA	(400	)	IN 92-103	2	18	14	28	15	15	
Spontaneous tumor pct: <= 1%	in ctrl. -		Total	-	1	0	0	0	0	
BONE MARROW	(7	)	FA 96	1	0	1	0	0	0	1.000 0.829 1.000
X-HISTIOCYTIC SARCOMA	(328	)	FA 96	2	29	30	36	32	30	
Spontaneous tumor pct: <= 1%	in ctrl. -		Total	-	0	1	0	0	0	

BRAIN	(9	)	IN 79-91	1	1	0	0	0	0	1.000	0.948	1.000
M-ASTROCYTOMA	(48	)	IN 79-91	2	15	15	10	13	15			
			IN 104-106	1	0	1	0	0	0			
			IN 104-106	2	15	19	15	21	20			
			FA 96	1	1	0	0	0	0			
			FA 96	2	28	31	36	32	30			
Spontaneous tumor pct: 2%	in ctrl.	-	Total	-	2	1	0	0	0			
BRAIN	(9	)	FA 74	1	0	0	0	1	0	0.398	0.341	1.000
M-EPENDYMOMA	(518	)	FA 74	2	54	54	55	54	53			
Spontaneous tumor pct: <= 1%	in ctrl.	-	Total	-	0	0	0	1	0			