

MPI Research Study Number 2265-001
A 104-Week Historical Control Oncogenicity Study with Interim Necropsies in Han Wistar Rats

Summary of Microscopic Observations - FEMALE
Terminal

Tissue Observation	Severity	Group 1	
		DOS	SNC
Number of Animals Examined		19	51
adrenal glands		(19)	(51)
adenoma, cortical, benign, primary		0	1
angiectasis/cystic degeneration, focal cortical		11	41
	- minimal	1	10
	- mild	8	30
	- moderate	0	1
	- severe	2	0
hyperplasia, focal cortical		1	6
	- minimal	0	3
	- mild	0	3
	- severe	1	0
hyperplasia, focal medullary		4	28
	- minimal	3	23
	- mild	1	5
hypertrophy, focal cortical	- minimal	0	2
lymphoma, malignant, multicentric		2	0
mineralization	- minimal	0	1
pheochromocytoma, benign, primary		2	1
within normal limits		6	4
aorta		(19)	(51)
mineralization	- mild	1	0

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		Group 1	
Tissue			
Observation	Severity	DOS	SNC
Number of Animals Examined		19	51
aorta		(19)	(51)
within normal limits		18	51
bile duct, extrahepatic		(0)	(2)
dilation		0	2
		- mild	
bone marrow, femur		(19)	(51)
hyperplasia, mixed		1	1
lymphoma, malignant, multicentric		2	0
within normal limits		16	50
		- mild	
bone marrow, sternum		(19)	(51)
hyperplasia, mixed		1	1
lymphoma, malignant, multicentric		2	0
within normal limits		16	50
		- mild	
bone, femur		(19)	(51)
within normal limits		19	51
bone, sternum		(19)	(51)
within normal limits		19	51
brain		(19)	(51)
carcinoma, pars distalis, malignant, secondary		0	1

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Tissue Observation	Severity	Group 1	
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Number of Animals Examined		19	51
brain		(19)	(51)
compression/hydrocephalus (pituitary tumor)		7	13
	- minimal	0	1
	- mild	0	1
	- moderate	7	11
granular cell tumor, benign, primary		0	1
granular cell tumor, malignant, primary		1	0
lymphoma, malignant, multicentric		1	0
within normal limits		10	38
cavity, oral		(1)	(2)
erosion/ulcer	- mild	1	0
inflammation, subacute/chronic	- mild	0	1
keratoacanthoma, benign, primary		0	1
clitoral glands		(19)	(49)
carcinoma, squamous cell, malignant, primary		1	0
dilatation/inflammation		4	11
	- minimal	0	1
	- mild	2	9
	- moderate	2	1
infiltration, mononuclear cell	- minimal	1	0
within normal limits		13	38

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Tissue			
Observation	Severity	DOS	SNC
Number of Animals Examined		19	51
esophagus		(19)	(51)
within normal limits		19	51
eyes		(19)	(51)
degeneration/atrophy, retina, bilateral		0	2
degeneration/atrophy, retina, unilateral		0	7
		- mild	
		0	2
		- mild	
		0	3
		- moderate	
		0	2
swelling, lens fibers		0	5
		- minimal	
		0	1
		- mild	
		0	3
		- moderate	
		0	1
within normal limits		19	40
eyes, optic nerves		(19)	(51)
within normal limits		19	51
galt		(19)	(51)
lymphoma, malignant, multicentric		1	0
within normal limits		18	51
harderian glands		(19)	(51)
atrophy		0	2
		- mild	

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Tissue Observation	Severity	Group 1	
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Number of Animals Examined		19	51
harderian glands		(19)	(51)
hyperplasia, focal	- minimal	0	1
infiltration, mononuclear cell within normal limits	- minimal	0	1
		19	47
heart		(19)	(51)
cardiomyopathy		13	35
	- minimal	8	30
	- mild	4	5
	- moderate	1	0
mineralization within normal limits	- mild	1	0
		6	16
joint, tibiofemoral		(19)	(51)
degenerative joint disease		0	6
	- mild	0	5
	- moderate	0	1
within normal limits		19	45
kidneys		(19)	(51)
calculus/calculi	- minimal	0	1
dilation, pelvic	- minimal	2	2
lymphoma, malignant, multicentric		2	0

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Tissue Observation	Severity	Group 1	
		DOS	SNC
Number of Animals Examined		19	51
kidneys		(19)	(51)
mineralization		8	32
	- minimal	4	25
	- mild	4	7
nephropathy, chronic progressive		9	42
	- minimal	4	28
	- mild	3	12
	- moderate	0	1
	- severe	2	1
pyelitis		0	2
	- minimal	0	1
	- moderate	0	1
within normal limits		4	4
lacrimal glands, exorbital		(19)	(51)
metaplasia, harderian		1	9
	- minimal	1	7
	- mild	0	2
within normal limits		18	42
large intestine, cecum		(19)	(51)
leiomyosarcoma, malignant, primary		0	1
within normal limits		19	50

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Tissue Observation	Severity	Group 1	
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Number of Animals Examined		19	51
large intestine, colon		(19)	(51)
within normal limits		19	51
large intestine, rectum		(19)	(51)
within normal limits		19	51
larynx		(19)	(51)
within normal limits		19	51
liver		(19)	(51)
adenoma, hepatocellular, benign, primary		0	1
cholangioma, benign, primary		1	0
cyst, biliary		0	2
	- minimal	0	1
	- moderate	0	1
degeneration, cystic, focal	- minimal	1	0
focus of cellular alteration, basophilic		0	11
	- minimal	0	8
	- mild	0	3
focus of cellular alteration, clear		3	6
	- minimal	2	3
	- mild	0	3
	- moderate	1	0
hematopoiesis, extramedullary	- minimal	1	6

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Tissue Observation	Severity	Group 1	
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Number of Animals Examined		19	51
liver		(19)	(51)
hemorrhage	- mild	0	1
hyperplasia, bile duct		2	23
	- minimal	1	17
	- mild	1	5
	- moderate	0	1
infiltration, mononuclear cell		5	13
	- minimal	5	12
	- mild	0	1
lymphoma, malignant, multicentric		3	0
necrosis, focal	- mild	0	1
vacuolation, increased lipid	- moderate	0	1
vacuolation, periportal	- mild	1	0
within normal limits		6	16
lung		(19)	(51)
granuloma, foreign body	- moderate	0	1
histiocytosis, alveolar		6	18
	- minimal	5	7
	- mild	1	10
	- moderate	0	1
hyperplasia, bronchiolar-alveolar	- minimal	0	1
inflammation, granulomatous	- minimal	1	0
inflammation, subacute/chronic	- minimal	0	1

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Terminal

		Group 1	
Tissue	Severity	DOS	SNC
Observation			
Number of Animals Examined		19	51
lung		(19)	(51)
lymphoma, malignant, multicentric		2	0
metaplasia, osseous	- minimal	0	1
mineralization	- mild	1	0
pneumonitis, uremic	- mild	1	0
within normal limits		11	32
lymph node, axillary		(3)	(7)
within normal limits		3	7
lymph node, hepatic		(0)	(1)
within normal limits		0	1
lymph node, iliac		(1)	(1)
within normal limits		1	1
lymph node, inguinal		(0)	(2)
within normal limits		0	2
lymph node, mandibular		(19)	(51)
lymphoma, malignant, multicentric		1	0
within normal limits		18	51

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Number of Animals Examined		19	51
lymph node, mediastinal		(0)	(1)
within normal limits		0	1
lymph node, mesenteric		(19)	(51)
depletion, lymphoid, generalized	- severe	1	0
dilation, sinus	- moderate	1	0
erythrocytosis/erythrophagocytosis, sinus	- mild	2	1
hyperplasia, lymphocyte/plasmacyte, medulla	- mild	0	1
lymphoma, malignant, multicentric		1	0
within normal limits		16	49
mammary gland		(19)	(51)
adenocarcinoma, malignant, primary		1	7
adenoma, benign, primary		0	4
dilation, gland/lumen		1	4
	- mild 1	3	
	- moderate	0	1
fibroadenoma, benign, primary		4	11
hyperplasia, lobular		7	29
	- minimal 2	11	
	- mild 3	14	
	- moderate	2	2
	- severe 0	2	
inflammation, granulomatous	- mild	1	0

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Terminal

Tissue Observation	Severity	Group 1	
		DOS	SNC
Number of Animals Examined		19	51
mammary gland		(19)	(51)
within normal limits		8	12
mesentery/peritoneum		(3)	(4)
hemorrhage	- moderate	1	0
lipoma, benign, primary		1	1
necrosis, fat		1	3
	- mild	1	0
	- moderate	0	3
multicentric neoplasm		(4)	(2)
hemangiosarcoma, malignant, multicentric		1	1
lymphoma, malignant, multicentric		3	1
nerve, sciatic		(19)	(51)
degeneration, axonal/myelin		9	42
	- minimal	9	41
	- mild	0	1
within normal limits		10	9
nose, level a		(19)	(51)
within normal limits		19	51

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		DOS	SNC
Number of Animals Examined		19	51
nose, level b		(19)	(51)
within normal limits		19	51
nose, level c		(19)	(51)
fungus/yeast	- moderate	0	1
within normal limits		19	50
nose, level d		(19)	(51)
lymphoma, malignant, multicentric		1	0
within normal limits		18	51
ovaries		(19)	(51)
cyst		0	2
	- moderate	0	1
	- severe 0	1	
hyperplasia, sex-cord/stromal		0	3
	- mild 0	2	
	- severe 0	1	
lipoma, benign, primary		0	1
sex-cord/stromal tumor, malignant, primary		0	4
within normal limits		19	42
oviducts		(19)	(51)
sex-cord/stromal tumor, malignant, secondary		0	1

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Tissue Observation	Severity	Group 1	
		DOS	SNC
Number of Animals Examined		19	51
oviducts		(19)	(51)
within normal limits		19	50
pancreas		(19)	(51)
adenoma, islet cell, benign, primary		0	1
atrophy, acinar	- minimal	1	0
hyperplasia, acinar cell, focal	- mild	1	0
lipomatosis	- mild	3	2
within normal limits		14	48
parathyroid glands		(15)	(38)
hyperplasia, focal	- mild	0	1
within normal limits		15	37
pharynx		(19)	(51)
within normal limits		19	51
pituitary gland		(19)	(51)
adenoma, pars distalis, benign, primary		11	32
carcinoma, pars distalis, malignant, primary		0	1
hyperplasia, focal, pars distalis		2	10
	- minimal	2	2
	- mild	0	7
	- moderate	0	1

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Tissue Observation	Severity	Group 1	
		DOS	SNC
Number of Animals Examined		19	51
pituitary gland		(19)	(51)
hyperplasia, pars intermedia	- moderate	0	1
within normal limits		6	9
salivary gland, mandibular		(19)	(51)
within normal limits		19	51
salivary gland, parotid		(19)	(51)
atrophy		1	1
- mild	1	0	
- moderate		0	1
within normal limits		18	50
salivary gland, sublingual		(19)	(51)
mineralization	- moderate	1	0
within normal limits		18	51
skeletal muscle, biceps femoris		(19)	(51)
degeneration/necrosis, myofiber	- minimal	1	0
hemangiosarcoma, malignant, multicentric		1	0
within normal limits		17	51
skin		(19)	(51)
erosion/ulcer	- moderate	2	0

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Tissue Observation	Severity	Group 1	
		DOS	SNC
Number of Animals Examined		19	51
skin		(19)	(51)
inflammation, subacute/chronic within normal limits	- moderate	1 17	0 51
skin, subcutis		(1)	(2)
hemangiosarcoma, malignant, multicentric		0	1
lipoma, benign, primary		0	1
schwannoma, malignant, primary		1	0
small intestine, duodenum		(19)	(51)
within normal limits		19	51
small intestine, ileum		(19)	(51)
within normal limits		19	51
small intestine, jejunum		(19)	(51)
dilation	- severe	0	1
erosion/ulcer	- mild	0	1
within normal limits		19	50
spinal cord, cervical		(19)	(51)
lymphoma, malignant, multicentric		1	0
within normal limits		18	51

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Tissue Observation	Severity	Group 1	
		DOS	SNC
Number of Animals Examined		19	51
spinal cord, lumbar		(19)	(51)
lymphoma, malignant, multicentric		1	0
within normal limits		18	51
spinal cord, thoracic		(19)	(51)
lymphoma, malignant, multicentric		1	0
within normal limits		18	51
spleen		(19)	(51)
hematopoiesis, extramedullary, increased		8	24
- minimal		4	19
- mild		3	4
- moderate		1	1
lymphoma, malignant, multicentric		3	0
within normal limits		8	27
stomach, glandular		(19)	(51)
within normal limits		19	51
stomach, nonglandular		(19)	(51)
carcinoma, squamous cell, malignant, primary		0	1
erosion/ulcer	- minimal	0	1
hyperplasia, squamous cell	- mild	1	1
within normal limits		18	49

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Tissue Observation	Severity	Group 1	
		DOS	SNC
Number of Animals Examined		19	51
thymus		(19)	(51)
depletion, lymphoid, generalized		16	41
	- minimal	2	1
	- mild	2	12
	- moderate	9	25
	- severe	3	3
hyperplasia, epithelial cell		2	20
	- minimal	1	12
	- mild	1	8
lymphoma, malignant, multicentric		1	0
thymoma, benign, primary		1	5
within normal limits		1	3
thyroid gland		(19)	(51)
adenoma, c-cell, benign, primary		0	9
adenoma, follicular cell, benign, primary		0	4
hemorrhage	- mild	0	1
hyperplasia, c-cell, diffuse		0	2
	- minimal	0	1
	- mild	0	1

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Number of Animals Examined		19	51
thyroid gland		(19)	(51)
hyperplasia, c-cell, focal		2	18
	- minimal	0	10
	- mild	1	7
	- moderate	1	1
hyperplasia, follicular cell within normal limits	- mild	0	1
		17	20
tongue		(19)	(51)
mineralization, vascular within normal limits	- minimal	1	0
		18	51
tooth/teeth		(1)	(1)
odontodysplasia		1	1
	- mild	0	1
	- moderate	1	0
trachea		(19)	(51)
within normal limits		19	51
ureters		(19)	(50)
dilation	- severe	0	1
inflammation, subacute/chronic	- moderate	0	1
within normal limits		19	49

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Tissue Observation	Severity	Group 1	
		DOS	SNC
Number of Animals Examined		19	51
urinary bladder		(19)	(51)
within normal limits		19	51
uterus with cervix		(19)	(51)
adenocarcinoma, malignant, primary		0	1
adenomyosis	- mild	0	1
cyst		0	4
	- mild	0	2
	- moderate	0	1
	- severe	0	1
dilation, gland/lumen	- mild	1	0
hyperplasia, cystic endometrial		2	11
	- minimal	1	5
	- mild	1	5
	- moderate	0	1
hyperplasia, squamous cell		0	3
	- mild	0	2
	- moderate	0	1
lymphoma, malignant, multicentric		0	1
polyp, stromal, benign, primary		2	6
within normal limits		15	29

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		DOS	SNC
Number of Animals Examined		19	51
vagina		(19)	(51)
within normal limits		19	51
zymbal's gland		(19)	(51)
within normal limits		19	51

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