

METHODS

Rat Studies

Estimation of Human Effective Doses.

Rats (3 males and 3 females per data point) were injected with ~18.5 MBq of ^{18}F -FPyKYNE-losartan (at time of first injection) into tail vein then sacrificed by decapitation at 5, 15, 30 and 60 min. Blood samples (~1.5 mL) were obtained from the trunk and urine was collected by a syringe. Whole tissues were dissected out, counted for activity (decay-corrected) along with aliquots of the injected solution as standards, and then weighed. Data were calculated as %ID/tissue and %ID/g of tissue (21,25). Radioactivity in the carcass was included as part of the remainder of body radioactivity. Time-integrated activity coefficients (Residence times) ($\text{Bq}\cdot\text{h}/\text{Bq}$) were obtained by exponential modeling and integration of organ activity curves vs time. The residence times were converted into human residence times by the Feller equation (26) and entered into the OLINDA/EXM software to obtain the organ absorbed doses. The effective dose (ED) was calculated using the ICRP Publication 103 and 60 tissue weighting factors using the procedure by Hunter et al. (27). Safety limits were applied as published in FDA regulations (28).

SUPPLEMENTAL TABLE 1

Whole body biodistribution of ¹⁸F-FPyKYNE-losartan in Sprague-Dawley rats

Organ or Tissue	Time (min)								
	5		15		30		60		
	% ID/ Organ or Tissue								
Brain	1.00E-02	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
Eye	1.00E-02	0.00E+00	1.00E-02	0.00E+00	1.00E-02	0.00E+00	0.00E+00	0.00E+00	0.00E+00
Thyroid	5.00E-02	1.00E-02	3.00E-02	1.00E-02	2.00E-02	2.00E-02	2.00E-02	0.00E+00	0.00E+00
Thymus	2.00E-02	0.00E+00	1.00E-02	0.00E+00	1.00E-02	0.00E+00	0.00E+00	0.00E+00	0.00E+00
Heart	9.00E-02	3.00E-02	3.00E-02	0.00E+00	1.00E-02	0.00E+00	1.00E-02	0.00E+00	0.00E+00
Lung	3.10E-01	5.00E-02	1.40E-01	2.00E-02	8.00E-02	1.00E-02	4.00E-02	2.00E-02	2.00E-02
Spleen	9.00E-02	4.00E-02	3.00E-02	3.00E-02	3.00E-02	2.00E-02	2.00E-02	1.00E-02	1.00E-02
Pancreas	2.30E-01	2.50E-01	1.40E-01	1.30E-01	1.20E-01	6.00E-02	6.00E-02	4.00E-02	4.00E-02
Esophagus	1.00E-01	3.00E-02	5.00E-02	3.00E-02	1.30E-01	1.30E-01	3.00E-02	1.00E-02	1.00E-02
Stomach Contents	3.00E-02	3.00E-02	8.00E-02	8.00E-02	2.00E-02	1.00E-02	2.00E-02	2.00E-02	2.00E-02
Stomach Wall	9.00E-02	3.00E-02	1.20E-01	8.00E-02	6.00E-02	2.00E-02	3.00E-02	2.00E-02	2.00E-02
LLI Contents	1.00E-02	1.00E-02	1.00E-02	1.00E-02	2.00E-02	2.00E-02	2.00E-02	3.00E-02	3.00E-02
LLI Wall	7.00E-02	3.00E-02	5.00E-02	4.00E-02	3.00E-02	1.00E-02	1.00E-02	1.00E-02	1.00E-02
ULI Contents	8.00E-02	9.00E-02	9.20E-01	1.52E+00	8.00E-02	6.00E-02	2.82E+00	4.68E+00	4.68E+00
ULI Wall	9.00E-02	6.00E-02	1.40E-01	1.50E-01	4.00E-02	1.00E-02	4.60E-01	7.70E-01	7.70E-01
Small Intestine Contents	8.10E-01	9.90E-01	4.57E+00	5.02E+00	2.56E+00	3.01E+00	4.41E+00	7.44E+00	7.44E+00
Small Intestine Wall	3.90E-01	2.10E-01	7.40E-01	8.10E-01	3.60E-01	2.70E-01	1.57E+00	2.64E+00	2.64E+00
Bladder	7.00E-02	4.00E-02	3.00E-01	2.70E-01	1.80E-01	1.30E-01	1.10E-01	8.00E-02	8.00E-02
Red Marrow	3.00E-02	2.00E-02	2.00E-02	1.00E-02	5.00E-02	4.00E-02	2.00E-02	3.00E-02	3.00E-02
Bone	3.00E-02	1.00E-02	2.00E-02	0.00E+00	2.00E-02	1.00E-02	3.00E-02	2.00E-02	2.00E-02
Muscle	2.00E-02	0.00E+00	2.00E-02	1.00E-02	2.00E-02	1.00E-02	2.00E-02	1.00E-02	1.00E-02
Mammary Gland	3.00E-02	0.00E+00	4.00E-02	2.00E-02	6.00E-02	0.00E+00	1.00E-02	2.00E-02	2.00E-02
Ovary	1.00E-01	1.00E-02	4.00E-02	2.00E-02	3.00E-02	2.00E-02	2.00E-02	0.00E+00	0.00E+00
Uterus	2.00E-02	0.00E+00	2.00E-02	1.00E-02	3.00E-02	2.00E-02	3.00E-02	2.00E-02	2.00E-02
Testis	3.00E-02	1.00E-02	3.00E-02	1.00E-02	4.00E-02	3.00E-02	2.00E-02	1.00E-02	1.00E-02
Adrenal Gland	1.20E-01	4.00E-02	4.00E-02	2.00E-02	3.00E-02	2.00E-02	3.00E-02	2.00E-02	2.00E-02
Kidney	2.03E+00	6.00E-01	9.30E-01	1.70E-01	3.30E-01	1.20E-01	1.10E-01	6.00E-02	6.00E-02
Liver	7.89E+01	1.79E+01	8.94E+01	2.29E+01	7.11E+01	1.48E+01	6.67E+01	1.35E+01	1.35E+01
Urine	5.60E-01	7.90E-01	6.30E-01	3.00E-01	6.10E-01	5.90E-01	1.42E+00	1.27E+00	1.27E+00
Blood	1.30E-01	4.00E-02	4.00E-02	1.00E-02	3.00E-02	0.00E+00	1.00E-02	0.00E+00	0.00E+00

3 males and 3 females per time point

Data are expressed as mean % injected dose (%ID) per organ or tissue ± SD.

LLI= Lower Large intestine; ULI= Upper Large Intestine.

SUPPLEMENTAL TABLE 2

Estimated effective doses for administration of ¹⁸F-FPyKYNE-losartan to humans

Organ	Male			Female		
	Equivalent Dose	Weighted	Weighted	Equivalent Dose	Weighted	Weighted
	to Target Organ mSv/MBq	Equivalent Dose ICRP 60	Equivalent Dose ICRP 103	to Target Organ mSv/MBq	Equivalent Dose ICRP 60	Equivalent Dose ICRP 103
Adrenals	4.34E-02	2.17E-04	4.01E-04	3.80E-02	1.90E-04	3.51E-04
Brain	1.92E-03	9.60E-06	1.92E-05	1.08E-03	5.40E-06	1.08E-05
Mammary Glands	5.24E-03	2.62E-04		1.37E-02	6.85E-04	1.64E-03
Gallbladder	4.17E-02		3.85E-04	4.15E-02		3.83E-04
LLI	1.05E-02	1.26E-03		6.42E-03	7.70E-04	
SI	1.51E-02	7.55E-05	1.39E-04	1.21E-02	6.05E-05	1.12E-04
Stomach	1.08E-02	1.30E-03	1.30E-03	1.14E-02	1.37E-03	1.37E-03
ULI	5.55E-02	2.78E-04		1.62E-02	8.10E-05	
Heart Wall	1.33E-02		1.23E-04	1.41E-02		1.30E-04
Kidneys	1.97E-02	9.85E-05	1.82E-04	1.84E-02	9.20E-05	1.70E-04
Liver	2.15E-01	1.08E-02	8.60E-03	2.46E-01	1.23E-02	9.84E-03
Lungs	1.13E-02	1.36E-03	1.36E-03	1.21E-02	1.45E-03	1.45E-03
Muscle	8.31E-03	4.16E-05	7.67E-05	7.47E-03	3.74E-05	6.90E-05
Ovaries				1.31E-02	2.62E-03	1.05E-03
Pancreas	4.82E-02	2.41E-04	4.45E-04	7.72E-02	3.86E-04	7.13E-04
Red Marrow	3.89E-02	4.67E-03	4.67E-03	1.68E-02	2.02E-03	2.02E-03
Osteogenic Cells	3.06E-02	3.06E-04	3.06E-04	1.71E-02	1.71E-04	1.71E-04
Skin	4.02E-03	4.02E-05	4.02E-05	3.51E-03	3.51E-05	3.51E-05
Spleen	7.08E-03	3.54E-05	6.54E-05	7.76E-03	3.88E-05	7.16E-05
Testes	5.34E-03	1.07E-03	4.27E-04			
Thymus	5.16E-03	2.58E-05	4.76E-05	4.91E-03	2.46E-05	4.53E-05
Thyroid	1.48E-02	7.40E-04	5.92E-04	7.43E-03	3.72E-04	2.97E-04
Bladder	1.83E-01	9.15E-03	7.32E-03	9.21E-02	4.61E-03	3.68E-03
Uterus	1.70E-02	8.50E-05		2.25E-02	1.13E-04	2.08E-04
Colon			4.34E-03			1.44E-03
ED (mSv/MBq)		3.37E-02	3.38E-02		2.89E-02	2.74E-02