



Supplementary Information

Non-invasive assessment of a local overexpressed human Adenosine 2A Receptor with [¹⁸F]FLUDA in the heart of a transgenic mouse model by PET

Daniel Gündel ^{1*}, Thu Hang Lai ^{1,2}, Sladjana Dukic-Stefanovic ¹, Rodrigo Teodoro ¹, Winnie Deuther-Conrad ¹, Magali Toussaint ¹, Klaus Kopka ^{1,7}, Rareș-Petru Moldovan ¹, Peter Boknik ³, Britt Hofmann ⁴, Ulrich Gergs ⁵, Joachim Neumann ^{5, #} and Peter Brust ^{1, 6, #}

- ¹ Helmholtz-Zentrum Dresden-Rossendorf, Institute of Radiopharmaceutical Cancer Research, Department of Neuroradiopharmaceuticals, Research Site Leipzig, 04813 Leipzig, Germany; d.guendel@hzdr.de (D.G.), t.lai@hzdr.de (T.H.L.), s.dukic-stefanovic@hzdr.de (S.D.-S.), r.teodoro@hzdr.de (R.T.), w.deuther-conrad@hzdr.de (W.D.-C.), m.toussaint@hzdr.de (M.T.), k.kopka@hzdr.de (K.K.); r.moldovan@hzdr.de (R.P.M.); p.brust@hzdr.de (P.B.)
 - ² Department of Research and Development, ROTOP Pharmaka Ltd., Dresden, Germany; t.lai@hzdr.de (T.H.L.)
 - ³ University of Muenster, Institute for Pharmacology and Toxicology, Muenster, Germany; boknik@uni-muenster.de (P.Bo.)
 - ⁴ Martin Luther University of Halle-Wittenberg, Medical Faculty, Cardiac Surgery, Halle, Germany; britt.hofmann@uk-halle.de (B.H.)
 - ⁵ Martin Luther University of Halle-Wittenberg, Institute for Pharmacology and Toxicology, Halle, Germany; Ulrich.gergs@medizin.uni-halle.de (U.G.), joachim.neumann@medizin.uni-halle.de (J.N.)
 - ⁶ The Lübeck Institute of Experimental Dermatology, University Medical Center Schleswig-Holstein, 23562 Lübeck, Germany; p.brust@hzdr.de (P.B.)
 - ⁷ Technical University Dresden, School of Science, Faculty of Chemistry and Food Chemistry, Dresden, Germany (K.K.)
- * Correspondence: d.guendel@hzdr.de; Tel.: +49 341 234179 4615
authors contributed equally

Citation: Gündel, D.; Lai, T.H.; Dukic-Stefanovic, S.; Teodoro, R.; Deuther-Conrad, W.; Toussaint, M.; Kopka, K.; Moldovan, R.-P.; Boknik, P.; Hofmann, B.; et al. Non-Invasive Assessment of Locally Overexpressed Human Adenosine 2A Receptors in the Heart of Transgenic Mice. *Int. J. Mol. Sci.* **2022**, *23*, 1025. <https://doi.org/10.3390/ijms23031025>

Academic Editor: Katia Varani

Received: 21 December 2021

Accepted: 14 January 2022

Published: 18 January 2022

Publisher's Note: MDPI stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.



Copyright: © 2022 by the authors. Submitted for possible open access publication under the terms and conditions of the Creative Commons Attribution (CC BY) license (<https://creativecommons.org/licenses/by/4.0/>).

Table of content:

Figure S1: *In vitro* binding study of [¹⁸F]FLUDA to control tissue cryosections (muscle and lung).

Figure S2: Dynamic PET imaging analysis of the [¹⁸F]FLUDA in the blood compartment (Left ventricle) and the radiotracer uptake of the myocardium in WT (n = 6) and A_{2A}-AR TG (n = 6) mice.

Figure S3: *Ex vivo* autoradiographic analysis of [¹⁸F]FLUDA accumulation in heart.

Figure S4: Dynamic PET imaging analysis of the [¹⁸F]FLUDA in different tissues.

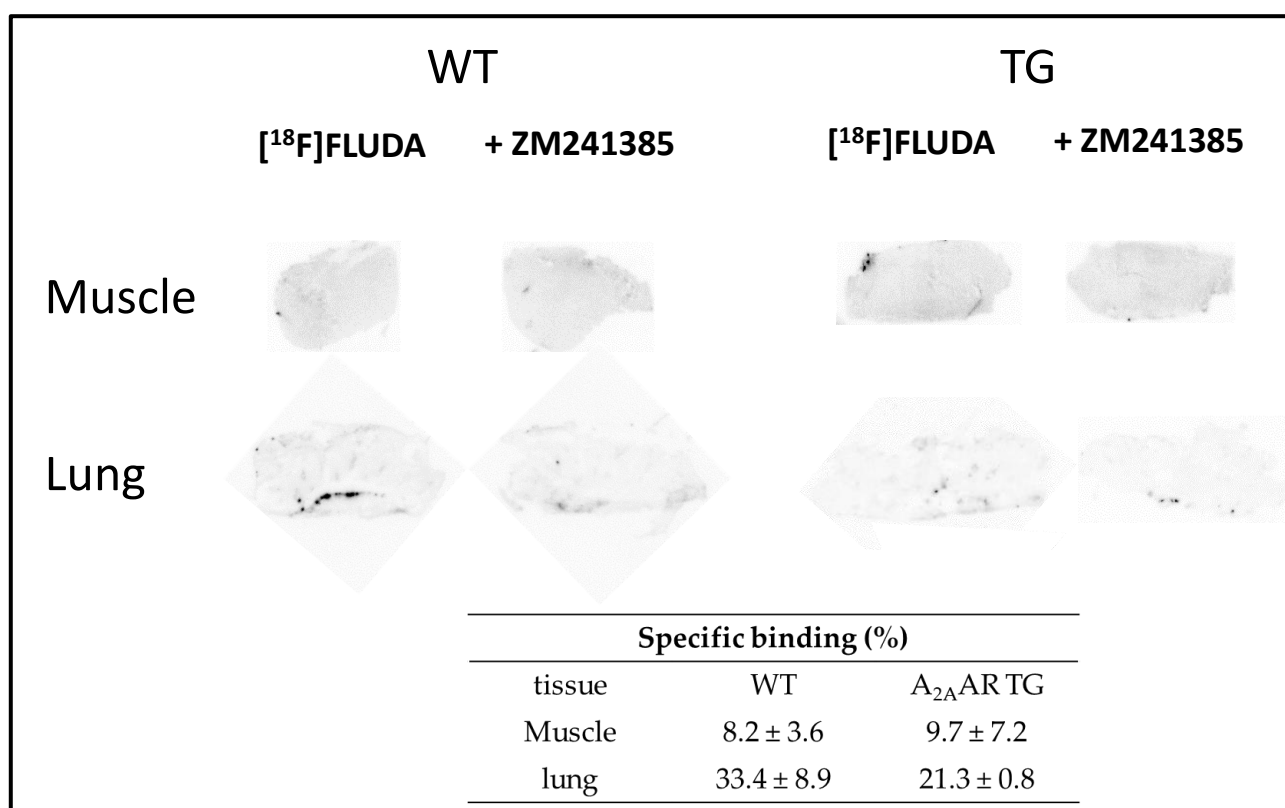


Figure S1. *In vitro* binding study of [¹⁸F]FLUDA to control tissue cryosections (muscle and lung) with and without 10 μM ZM241385 (each n = 2) to determine the specific binding of the radioligand.

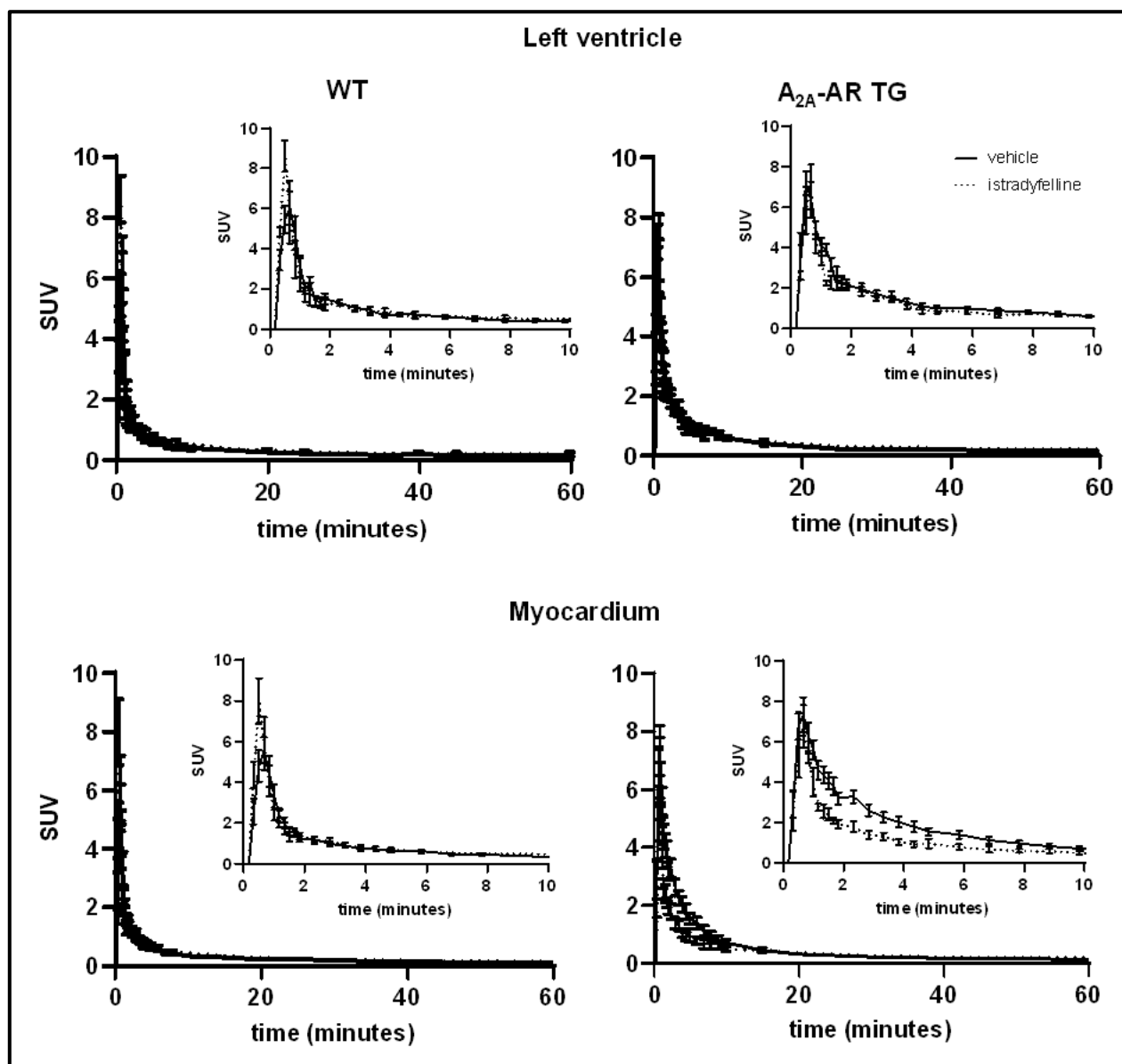


Figure S2. Dynamic PET imaging analysis of the [^{18}F]FLUDA concentration in the blood compartment (Left ventricle) and the radio-tracer uptake of the myocardium in WT ($n = 6$) and $\text{A}_{2\text{A}}\text{-AR TG}$ ($n = 6$) mice. The time activity curves after radiotracer administration are represented in mean activity concentrations as standardized uptake values ($\text{SUV}_{\text{mean}} \pm \text{SEM}$) in the delineated volume of interests of indicated tissue regions. Mice were pre-treated with vehicle or 1 mg/kg bodyweight istradefylline 10 minutes prior radiotracer application.

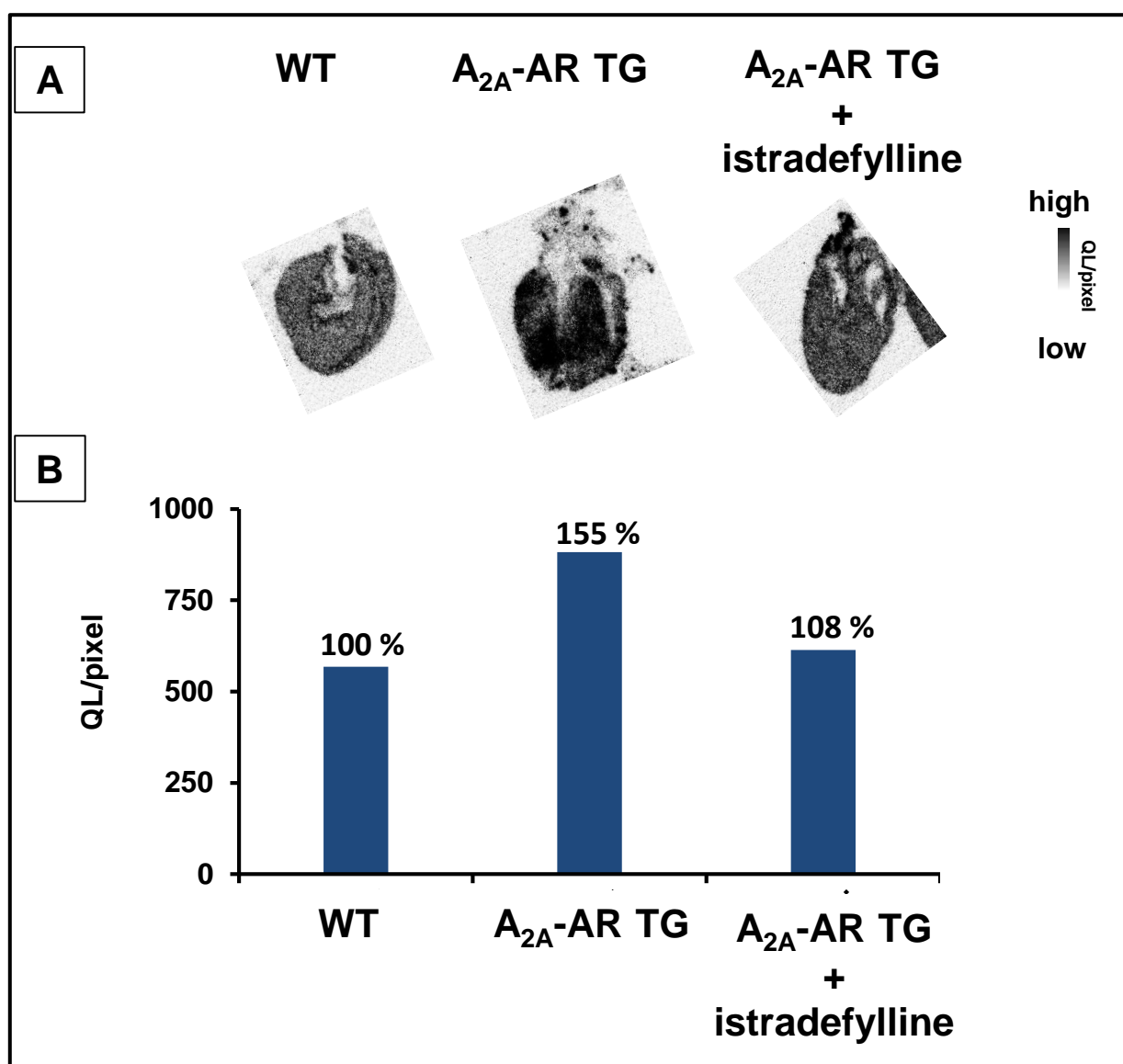


Figure S3. Exemplary *ex vivo* autoradiographic images (A) and the according analysis (B) of $[^{18}\text{F}]$ FLUDA accumulation in heart at 15 min p.i. of the radioligand in cryosections of murine heart (16 μm) of WT and A_{2A} -AR TG (with and without preadministration of istradefylline, $n=1$).

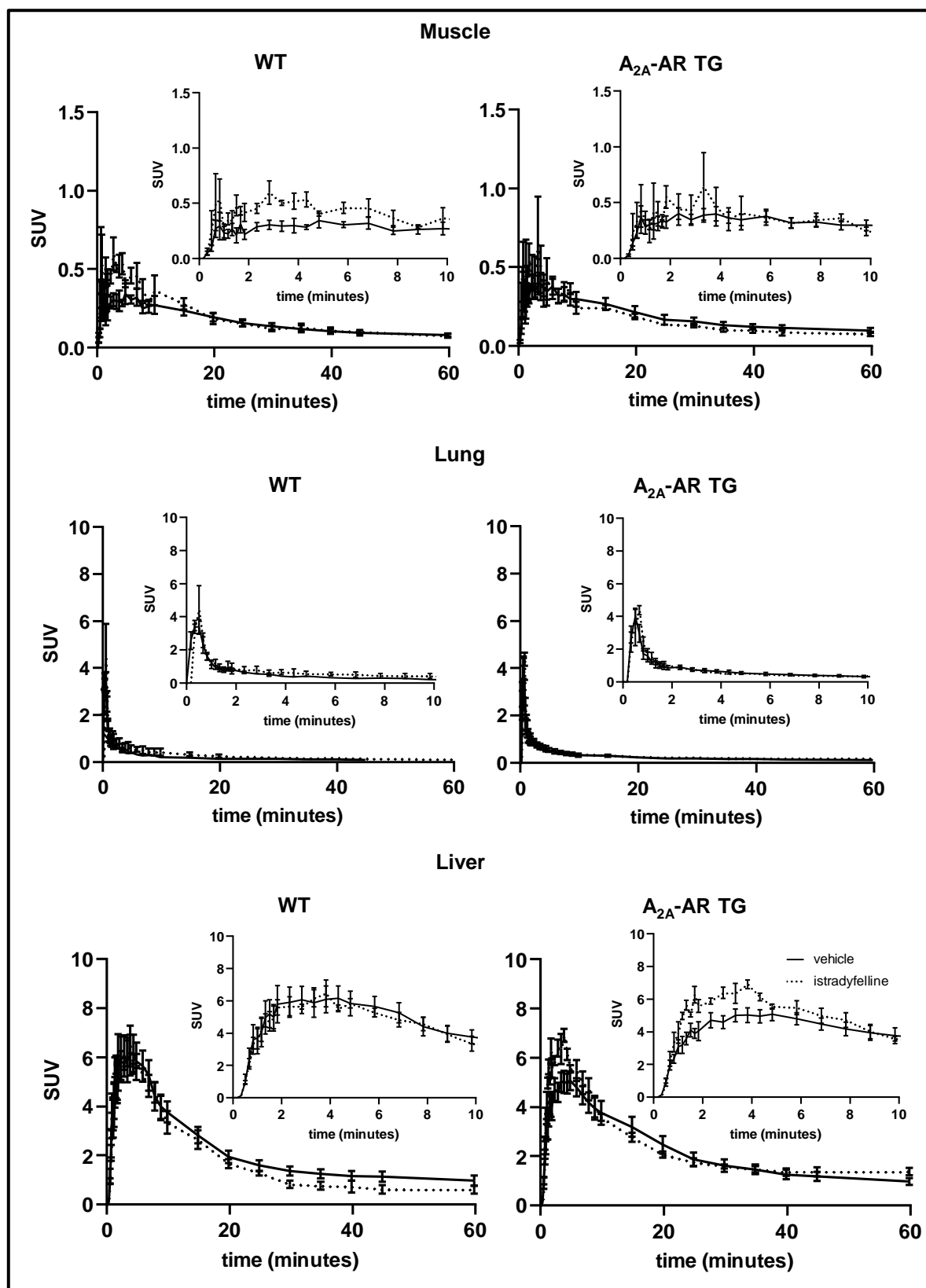


Figure S4. Dynamic PET imaging analysis of the [^{18}F]FLUDA concentration in the blood and of the radiotracer uptake of different tissues in WT ($n = 6$) and A_{2A} -AR TG ($n = 6$) mice. The time activity curves after radiotracer administration are represented in mean activity concentrations as standardized uptake values ($\text{SUV}_{\text{mean}} \pm \text{SEM}$) in the delineated volume of interests of indicated tissue regions. Mice were pre-treated with vehicle or 1 mg/kg bodyweight istradefylline 10 minutes prior radiotracer application.

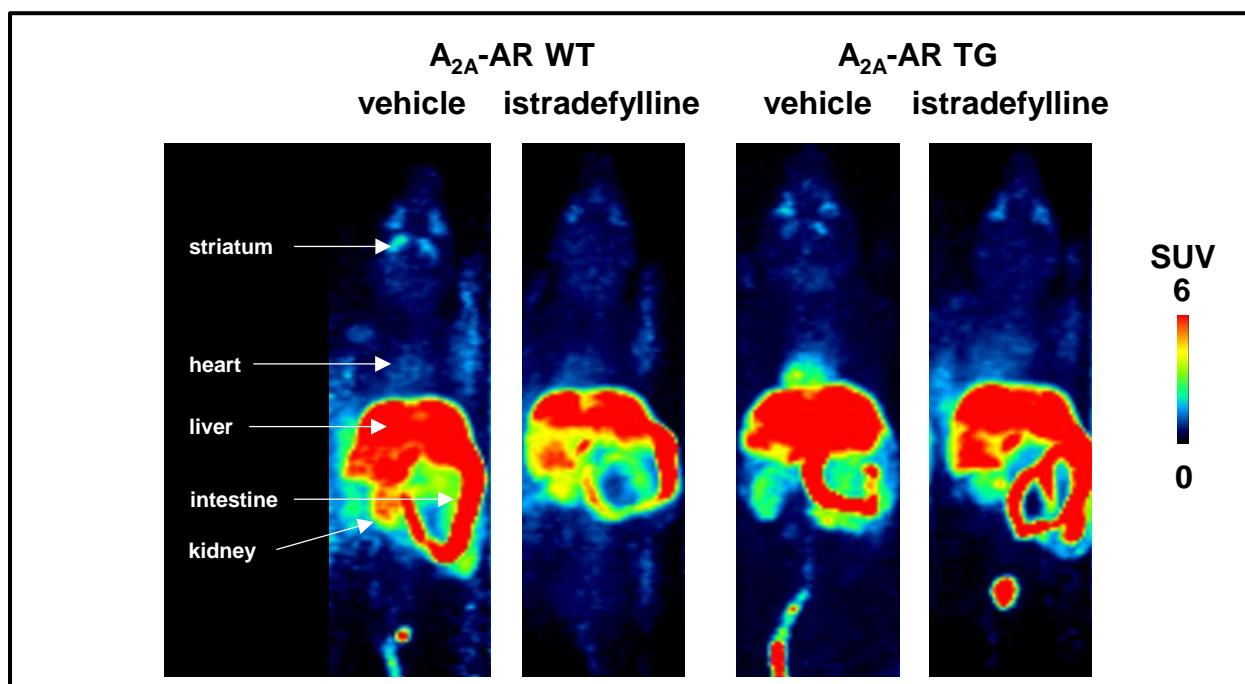


Figure S5. Representative averaged whole body maximum intensity projections (MIPs) from 1 to 10 min p.i. of the PET acquisition of [¹⁸F]FLUDA in WT and A_{2A}-AR TG with or without preadministration of istradefylline.