The choice of patients groups will benefit more from certain drug is very critical step in treatment success and reduce the toxicity and cost.Refinement : this principle is applied since they used noninvasive in vivo PET imaging The radiation exposure to the NSCLG was limited with safety with minimum adverse effectsOverall in my opinion the animals models selection was perfect and the NSCLC patients are good choices but there are a lots of things can be modified such as the sample size and randomaiztion to prevent baise and maybe to be more specific and accurate more studies on Non-rodent species is needed before clinical trials since Non-rodent species is more close to human physiology and bigger than Rodents since the size of the animals models consider as important factor.Both studies was mentioned the ethical approval and compliance with regulations and ethics The preclinical trial on animals supports the authors' conclusions which is demonstrated the ability to use a noninvasive immunotherapeutic-based imaging agent to monitor PD-1 localization and expression in vivo , and its statistically significant since the p-value less than 0.05 so there's a real uptake of the radiolabel drug by tissue.The clinical trial on NSCLC patients the 89Zr-pembrolizumab uptake was safe and that it was higher in patients with a response than in patients without a response, but this fnding was not statistically signicant due to small sample size so further studies are needed Replacement : this principle is not applied , since they used Humanized animal models (mice and rats) , I think the use of animals model is necessary to test the biodistribution, pharmacokinetics, and dosimetry in vivo and can't be replaced by other test such as vitro assays or in silico studies Reduction : no clear number of animals used but they mentioned the use of 4 animals in each.