Contribution ID: **47** Type: **not specified**

Consideration toward Safety Guidance for Targeted Alpha Therapy in Japan

Targeted alpha therapy (TAT) was reported both decreasing side effects and significant therapeutic efficacies in comparison with several conventional anti-tumor treatments. Although the TAT research project has also started in Japan to proceed with drug development, there is still no concrete evaluation standard to conduct non-clinical studies for TAT drug toward human clinical studies. Regulatory science for translational research of drug product under international standard is very important now. While watching the current progress on the TAT drug development and the several subjects clarified by the former TAT research, we have recently published our report on evaluation standard for non-clinical studies which is essentially necessary for first-in-human TAT studies in Japan1). We focused on both astatine 211At and actinium 225Ac as the alpha-emitters. We also discuss on initial human-dose and dose escalation, organ identification to suspect toxicity and evaluation items for monitoring upon considering physical half-lives, drug stabilities and accumulation into targeted cells. Both biodistribution analysis by PET or SPECT using complementary nuclide labeling agents and localization analysis by auto-radiography imaging for animal tissues using alpha-camera are very important for these purposes1). We also propose the selection method of TAT drug candidates which is satisfied with safety profile including delayed-type toxicities under our new evaluation system with histopathological examination in animal tissues which is also very important to deepen our understanding1).
Furthermore, dose escalation studies and their verification of accuracy using animal models will be established by our newly proposed dosimetric simulation which adopts reliable extrapolation to human trials2).
We expect this report can provide how to think about the non-clinical safety issues for development of new TAT drugs in advance.
Acknowledgement; This research is supported by the Program on Open Innovation Platform with Enterprises, Research Institute and Academia (OPERA) from Japan Science and Technology Agency (JST).
1)Tsuneo Yano, Koki Hasegawa, Akiko Hachisuka, Koichi Fukase, Yoko Hirabayashi, Discussion on Translational Research of Drug Product for Targeted Alpha Therapy –Part 1 –, PMDRS, 49(10), 676-684 (2018).
2)Tsuneo Yano, Koki Hasegawa, Tatsuhiko Sato, Akiko Hachisuka, Koichi Fukase, Yoko Hirabayashi, Discussion on Translational Research of Drug Product for Targeted Alpha Therapy –Part 2 –, PMDRS, 50(3), March 10th (2019).

Funding Agency

Japan Science and Technology Agency (JST)

Email Address

tyano@rcnp.osaka-u.ac.jp

Presentation Type

Contributed Oral

Primary author: Prof. YANO, Tsuneo (Osaka University)

Presenter: Prof. YANO, Tsuneo (Osaka University)