Clinical Development of Radiopharmaceuticals

Anthony Fotenos, MD, PhD
Lead Medical Officer, US Food and Drug Administration
Division of Imaging and Radiation Medicine (DIRM), Office of Specialty Medicine (OSM), Office of New Drugs (OND)
CDER | US FDA

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drug or biologic

emits nuclear particles or photons

radiopharmaceuticals

regulation from a clinical perspective

same way as any other pharmaceutical

CDER leads

regulations unique to radiopharmaceuticals

dosimetry

diagnostic radiopharmaceuticals

in vivo administration

diagnosis or monitoring

Code of Federal Regulations Title 21

Part 315

useful clinical information

reliable assessment of actual clinical status

anatomy

don’t require truthing methods

reader ratings improve

function or detection of disease

truthing method

Ga68 Dotatoc

neuroendocrine tumors

N = 177	NET status as identified by reader	Reference	
		Positive	Negative
Reader 1	Positive	121	5
	Negative	12	39
	Agreement (%)* (95% CI)**	91 (85, 95)	89 (75, 96)
Reader 2	Positive	120	6
	Negative	13	38
	Agreement (%)* (95% CI)**	90 (84, 95)	86 (73, 95)

Source: https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/210828s000lbl.pdf

Ga68 PSMA-11

prostate cancer

		Histopathology		Predictive value** (95% CI)
		Positive	Negative	
PET scan	Positive	14	9	PPV 61% (41%, 81%)
	Negative	16	84	NPV 84% (79%, 91%)
Total		30	93	
Diagnostic performance (95% CI)		Sensitivity 47% (29%, 65%)	Specificity 90% (84%, 96%)	

Source: https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/212642s000lbl.pdf

diagnostic radiopharmaceuticals to manage

feel, function, or survive

theranostic pair

therapeutic and parallel imaging

common mechanism

parallel imaging radiopharmaceutical = PIR

PIR efficacy endpoints

patient selection indication

reuse endpoints

agreement to PIR dosimetry

reader agreement

pre-specified sub-group analysis

fallback considerations

PIR development phases

early-phase range-finding

phase 3 statistical analysis plan

prescribing information

instruction for all oncology co-providers

Additional reading

- Efficacy considerations for U.S. Food and Drug Administration approval of diagnostic radiopharmaceuticals. J Nucl Med 2013; 54:1479–1484

- Recent advances in clinical trial design considerations in Thera“nostics”. Contemporary Clinical Trials 2020; 96:106100

- Theranostics: regulatory considerations for product development. FDA-SNMMI-NIH 2019 Workshop. https://s3.amazonaws.com/rdcms-snmmi/files/production/public/docs/pr/Theranostics%20Workshop_SNMMI%20AM%20CAT04_June%202019.pdf

- Enhancing development of novel technologies: radiopharmaceuticals and radiological devices. FDA-NRC 2020 Workshop. https://www.fda.gov/drugs/news-events-human-drugs/fda-nrc-workshop-enhancing-development-novel-technologies-radiopharmaceuticals-and-radiological