# PIVALATE ACHIEVES POSITIVE PHASE II DATA IN BRAIN METS TRIAL

*Presentation at a Joint Meeting of the European Organisation for Research and Treatment of Cancer (EORTC), the (USA) National Cancer Institute (NCI), and the America Association for Cancer Research (AACR) in Barcelona, Spain, 26-28 Oct 2022*

Imperial College London

RAD
RADIOPHARM THERANOSTICS

# PIVALATE DELIVERS POSITIVE PHASE II DATA IN BRAIN METS TRIAL



## *Background*

- F18-Pivalate is a novel radiotracer for the detection, characterisation and progression monitoring of glioblastoma and brain metastases
- F18-Pivalate targets fatty acid synthetase, selectively overexpress by tumors, but not by normal brain cells
- Pivalate has unique Mechanism of Action and potentially transformational approach
- Approximately 20-40% of patients with cancer will develop metastatic cancer to the brain during the course of their illness
- Currently available technologies such as PET FDG and MRI, have limitations, due to necrotic, inflammatory and high sugar uptake confounding factors. F18-Pivalate attempts to overcome these limitations.

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## RAD 101 Phase II trial overview

- The RAD 101 Phase IIa open label trial performed F18-Pivalate PET/MRI in patients with one or more cerebral metastases from different primary tumours of origin; breast, lung, melanoma and colorectal cancer

- The trial analysed:
  - whether F18-Pivalate uptake is higher over background in cerebral metastases, and
  - whether Steareotactic Radiosurgery (SRS) impacts F18-Pivalate uptake at early time points (4-8 weeks)

- Under the Phase IIa trial there were two cohorts of patients; 11 patients treatment naïve and 6 patients SRS treated (4-8 weeks post treatment). We present analysis of the first 17 scans (16 treatment naïve lesions and 8 radiotherapy treated lesions).

- Treatment naïve cohort is concluded, and results can be considered final; enrollment continues only in SRS treated patients

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## *RAD 101 Phase IIa Trial Results*

- Under the Phase IIa trial, F-18 Pivalate PET showed high uptake regardless of origin of primary tumor. This indicates that Pivalate can be used to detect & monitor cerebral metastases

- Patients without previous external beam radiation showed higher tumor uptake of the radiotracer, while previously treated patients show a trend towards lower uptake of the radiotracer

***The RAD 101 Phase II results are being presented at a Joint Meeting of the European Organisation for Research and Treatment of Cancer (EORTC), the (USA) National Cancer Institute (NCI), and the America Association for Cancer Research (AACR) in Barcelona, Spain, 26-28 Oct 2022***

| RAD CODE | MOLECULE | INDICATION | DX / TX | ISOTOPE | COUNTRY | PRECLINICAL | PHASE I | PHASE II | PHASE III | NOTES |
|---|---|---|---|---|---|---|---|---|---|---|
| RAD 101 | pivalate | Brain Mets | Dx | F18 | UK | → | → | → | | **Positive Phase II achieved** |

# PIVALATE DELIVERS POSITIVE PHASE II DATA IN BRAIN METS TRIAL

**Pivalate Platform Next Steps:**

- **RAD 101 (Diagnostic)**
  - Scientific Advisory Board to conclude detailed analysis of the Phase IIa data and ascertain the most appropriate use case in clinical practice
  - Meeting with FDA to determine regulatory pathway to accelerate development of Pivalate for imaging
- **RAD 102 (Therapeutic)**
  - Select final therapeutic candidate
  - Imaging Proof of Concept supports therapeutic development
  - Leverage Phase IIa imaging data for Therapeutic Phase I protocol in patients with brain mets and/or Glioblastoma

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# BRAIN METS MARKET OPPORTUNITY

Prostate cancer is a large radiopharmaceutical imaging indication that received FDA approval. We therefore see this as the best proxy in assessing Radiopharm's potential market opportunity for its brain mets indication

| Cancer type | New US Cases Per Annum | Eligible New Patients Per Annum | Price Per Dose | Potential market size[3] | Companies with Lead Products in Indication |
|---|---|---|---|---|---|
| Prostate | 248,000<br>*Source: SEER database - US incidence* | 170,000<br>***Source: IR LANTHEUS HOLDING 2021*** | USD$4,730<br>***Source: Taylor Collison*** | USD$804.1M | LANTHEUS<br>***USD$4.7B market cap[2]***<br>TELIX PHARMACEUTICALS<br>***A$1.7B market cap[2]*** |
| Brain Mets[1] | 390,000<br>*Source: SEER database - US incidence* | 265,000<br>***Management estimate: Assumed same proportion of eligible patients as prostate*** | USD$4,730<br>***Management estimate: Assumed same pricing as prostate*** | USD$1,253.5M | RAD RADIOPHARM THERANOSTICS<br>***A$42.1M market cap[2]*** |

[1] *Assumes RAD obtains FDA approval for F18-Pivalate and that price per dose is equivalent to Prostate Cancer Diagnostic Imaging Agent, Pylarify*

[2] *Market capitalisation as at 13 October 2022*

[3] *Equal to eligible new patients multiplied by price per dose*

# PIVALATE DELIVERS POSITIVE PHASE II DATA IN BRAIN METS TRIAL

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**18F-Fluoropivalate PET/MRI: imaging of treatment naïve patients and patients treated with radiosurgery**

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[2]Imperial College London, Brain Sciences, London, United Kingdom.

**Background:** Approximately 20-40% of patients with cancer will develop metastatic cancer to the brain during the course of their illness. The brain niche imposes metabolic constraints on tumour cells that metastasise to the organ involving utilisation of short chain fatty acids (SCFAs) in the presence of glucose (Mashimo et al Cell 2014). We developed $^{18}$F-fluoropivalate (FPIA), for imaging SCFA transcellular flux and showed high uptake in orthotopic human brain tumours in mice. In humans, FPIA was found to have favourable dosimetry - 0.0154 mSv/MBq. We hypothesised that FPIA uptake will be high in metastases regardless of primary tumour of origin and will decrease with treatment. In this interim analysis we ask a) whether FPIA uptake is higher over background in cerebral metastases, and b) whether Steareotactic Radiosurgery (SRS) impacts FPIA uptake at early time points (4-8 weeks) when changes in imaging outcome can influence future patient management; but for which a third of patients show pseudoprogression on magnetic resonance imaging (MRI) (Patel et al Am J Neuroradiol 2011).

**Methods:** We performed FPIA-PET/MRI in patient with one or more cerebral metastases from different primary tumour of origin: breast, lung, melanoma and colorectal cancer. There were two cohorts of patients, treatment naïve and SRS treated (4-8 weeks post treatment). We present analysis of the first 17 scans (16 treatment naïve lesions and 8 radiotherapy treated lesions).

**Results:** High contrast images were seen at the 60 min time-frame after radiotracer injection. The maximum standardised uptake (SUVmax) within lesions compared to the mean SUV of contralateral brain (SUVmean) was found to differ markedly: Mean ± SEM of 1.54 ± 0.11 vs 0.47 ±0.04 ($p < 0.0001$). The calculated Tumour-to-Background ratio (TBR; SUVmax in tumour/SUVmean in contralateral brain) ranged between 1.73 to 6.07 (Mean ± SEM of 3.85 ± 0.33) supporting the qualitative assertion of high image contrast in patients regardless of cancer of primary origin. Both the highest and lowest TBR values were derived from patients who presented with lung cancer primary tumours. TBR was lower in the cohort that received radiotherapy 2.92 ± 0.26 ($p = 0.074$) and comparatively, dynamic contrast enhanced (DCE)-Kep - symmetric exchange rate of MRI contrast agent across the capillary wall - was markedly lower in the same group.

**Conclusion:** FPIA PET shows high uptake regardless of primary tumour of origin, indicating that the tracer can be used to monitor cerebral metastases. At the time when only half of patients in the treatment group has completed their assessment, there was a trend towards lower uptake of the radiotracer at early time points after initiating radiotherapy. The decrease in FPIA may be due in part to decreases in cell viability or capillary wall changes.

# SIX PLATFORMS, 9 WELL DIFFERENTIATED MOLECULES

RAD
RADIOPHARM THERANOSTICS

## ONE OF THE DEEPEST PIPELINES IN RADIOPHARMACEUTICAL THERAPIES

### 4 Nano-mAbs
81 patients dosed

- ***4*** *Single chain mAbs*
- Imaging with Tc99
- Therapeutic with Re188 / Lu177

**POTENTIAL INDICATIONS**

**HER2+ Breast**
**PD-L1+ NSCLC**
**TROP2+ TNBC**
**PTK7+ Ovarian**

### Avb6 Integrin
88 patients dosed

- *Peptide molecule*
- Imaging with Ga68
- Therapeutic with Lu177

**POTENTIAL INDICATIONS**

**Pancreatic**
**Head & Neck**

### Pivalate
61 patients dosed

- *Small molecule*
- Imaging with F18
- Therapeutic with I131

**POTENTIAL INDICATIONS**

**Brain Metastasis**
**Glioblastoma**

### PSA-mAb

- *mAb*
- Imaging with Zr89
- Therapeutic with Ac225

**POTENTIAL INDICATIONS**

**Prostate cancer**

### DUNP19

- *mAb*
- Imaging with Cu-64
- Therapeutic with Lu177

**POTENTIAL INDICATIONS**

**Osteosarcoma**

### PTPm

- *Peptide molecule*
- Imaging with Ga-68
- Therapeutic with Lu-177

**POTENTIAL INDICATIONS**

**Glioblastoma**

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