



# **Novel Receptor Tyrosine Kinase Pathway Inhibitors for Targeted** Radionuclide Therapy of Glioblastoma

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## INTRODUCTION

Glioblastoma (GB) remains the most fatal brain tumor characterized by a high infiltration rate and treatment resistance. The median survival is approximately 14 months and less than 10% of patients living longer than 5 years from diagnosis. New treatment strategies are urgently needed and the future is **THERANOSTICS**.

RECEPTOR TYROSINE KINASE INHIBITORS FOR THE TREATMENT OF GLIOBLASTOMA





**THERANOSTICS** = combination of diagnostic molecular imaging with targeted therapy using the same agent. The theranostic agent thereby investigates the presence of a certain target on the tumour cells of the patient while the therapeutic version of the agent (commonly a radioactive derivative) binds to the same target and induces tumour cell death by emitting radiation,.



Mutations in **receptor tyrosine** kinases (RTKs) and aberrant activation of their intracellular signalling pathways have been linked malignant to transformation therapy and resistance and have driven the development of a new generation of drugs that block or attenuate RTK activity. Overexpression and/or mutation of RTKs is common in GB, and therefore kinase tyrosine receptor (RTKIs) inhibitors have been investigated to improve the dismal prognosis of GB in an effort evolve to into personalized targeted therapy strategy.

#### EXISTING GLIOBLASTOMA RECEPTOR TYROSINE KINASE RADIOPHARMACEUTICALS



#### SELECTED NEW PROMISING GLIOBLASTOMA RADIOPHARMACEUTICALS

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Proposed glioblastoma targeted radionuclide therapy agents

#### **METHODOLOGY**

Understanding cancer pathways in GB

#### Receptor tyrosine kinase pathway PATHWAYS

**Drug development** Receptor tyrosine kinase inhibitors

#### Drug radiolabelling

• Diagnostic radionuclide (e.g. <sup>68</sup>Ga, <sup>18</sup>F) • Therapeutic radionuclide (e.g. <sup>177</sup>Lu)

#### LABELLING

THERAPY

INHIBITORS

• Theranostic radionuclide (e.g. <sup>131</sup>I)

#### Nuclear imaging

Molecular target confirmation

• Predicting/monitoring tumour IMAGING response

### **Targeted radionuclide therapy (TRT)** • Patient-based treatment decisions • Reduced toxicity

**Receptor tyrosine kinase** inhibitors and radiopharmaceuticals



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