INPLASY

Theranostics of somatostatin receptors in the management of patients with neuroendocrine tumors: agonists versus antagonists A Systematic Review and Meta-Analysis

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ADMINISTRATIVE INFORMATION

Support - CSC(No.202208140021).

Review Stage at time of this submission - Formal screening of search results against eligibility criteria.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY2024120022

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 5 December 2024 and was last updated on 5 December 2024.

INTRODUCTION

Review question / Objective Neuroendocrine tumors (NETs) are a rare and heterogeneous class of neoplastic lesions. However, their prevalence has increased significantly over the past three decades. The treatment of these tumors has, at times, proven to be challenging. Improving diagnostic efficiency and treatment effectiveness is very important for patients with neuroendocrine tumors. Theranostic radiopharmaceutical approach combines diagnosis and treatment technology and has promising prospects in precision medicine, especially for the early diagnosis and treatment of tumors. Recently, researchers have identified the potential of radiolabeled somatostatin receptor (SSTR) antagonists in diagnosing and treating neuroendocrine tumors. Compared to agonists, radiolabeled somatostatin receptor (SSTR) antagonists exhibit superior characteristics in neuroendocrine tumors (NETs). We planned to compare somatostatin receptor antagonists and somatostatin receptor agonists in the theranostics of neuroendocrine tumors by meta-analysis
P: Patients with suspected Neuroendocrine tumor or patients with Neuroendocrine tumor;
I: Radiolabeled somatostatin receptor agonists or somatostatin receptor antagonists;
C: Histopathology, imaging, or clinical follow-up, RECIST1.1;
O: Diagnostic efficiency, disease control rate;
S: RCT, or cohort study, or case-control study.

Condition being studied Although NET is relatively rare, its prevalence has increased significantly over the past three decades. Theranostic radiopharmaceuticals based on somatostatin receptor agonists, such as [90Y]Y- or [177Lu]Lu-DOTATOC, [177Lu]Lu-DOTATATE, and [68Ga]Ga-DOTATOC and [68Ga]Ga-DOTATATE, in Its use in the diagnosis and treatment of patients with neuroendocrine tumors has previously been widespread in clinical practice and plays a key role in patient prognosis and quality of life. Recently

introduced SSTR antagonists, such as [68Ga]Ga-DOTA-JR11, have made significant progress in the field of SSTR targeting. Unlike agonists, antagonists generally do not induce internalization. Instead, they bind to the activated and inactive conformations of SSTR and dissociate more slowly than agonists. Therefore, radioactivity accumulates on the surface of tumor cells, but with greater intensity than the agonist.

METHODS

Search strategy The search keywords were as follows: (1) neuroendocrine tumors; (2) "theranostics" OR "treatment" OR "diagnosis"; (3) somatostatin receptor; (4) "antagonist" OR "agonist". Take the pubmed search query as an example:
((((("Neuroendocrine Tumors"[Mesh]) OR (((((Neuroendocrine Tumor[Title/Abstract]) OR (Tumor, Neuroendocrine[Title/Abstract])) OR (Tumors, Neuroendocrine[Title/Abstract])) OR (NETs[Title/Abstract])) OR (NET[Title/Abstract]))) AND (("Receptors, Somatostatin"[Mesh]) OR ((((((Somatostatin Receptor[Title/Abstract]) OR (Receptor, Somatostatin[Title/Abstract])) OR (Somatostatin Receptors[Title/Abstract])) OR (Receptors, Somatotropin Release Inhibiting Hormone[Title/Abstract])) OR (Receptors, SRIH[Title/Abstract])) OR (SRIH Receptors[Title/Abstract]))))) AND ((((((((((("agonists" [Subheading]) OR ("antagonists and inhibitors" [Subheading])) OR (((antagonists[Title/Abstract] AND inhibitors[Title/Abstract]) OR (antagonists[Title/Abstract])) OR (inhibitors[Title/Abstract]))) OR (("gallium Ga 68 dotatate" [Supplementary Concept]) OR ((((((((((((((dotatate gallium ga-68[Title/Abstract]) OR (gallium 68 DOTA-octreotide[Title/Abstract])) OR (gallium (68ga) dota-tate[Title/Abstract])) OR (gallium-dota-octreotate, ga-68[Title/Abstract])) OR (gallium dotatate, ga-68[Title/Abstract])) OR (gallium 68 dotatate[Title/Abstract])) OR (68Ga-DOTATATE[Title/Abstract])) OR (68gallium-DOTA-Tyr(3)-Thr(8)-octreotate[Title/Abstract])) OR (edotreotide gallium ga-68[Title/Abstract])) OR (gallium ga-68 edotreotide[Title/Abstract])) OR (gallium edotreotide ga-68[Title/Abstract])) OR (gallium ga 68-dotatoc[Title/Abstract])) OR (Ga-68 dota0-tyr3-octreotide[Title/Abstract])) OR (gallium Ga 68-edotreotide[Title/Abstract]))))) OR (("68Ga-DOTANOC" [Supplementary Concept]) OR (68Ga-DOTA-NOC[Title/Abstract])))) OR (("Ga(III)-DOTATOC" [Supplementary Concept]) OR (((67Ga-DOTATOC[Title/Abstract]) OR (gallium-68 DOTATOC[Title/Abstract])) OR (68Ga-DOTATOC[Title/Abstract]))))) OR (("lutetium Lu 177 dotatate" [Supplementary Concept]) OR (((((((177lutetium-DOTA-O-Tyr3-octreotate[Title/Abstract]) OR (lutetium 177Lu oxodotreotide[Title/Abstract])) OR (Lu-177 DOTATE[Title/Abstract])) OR (177Lu-DOTAOTyr3-octreotate[Title/Abstract])) OR (DOTATATE-177Lu[Title/Abstract])) OR (177Lu-DOTATATE[Title/Abstract])) OR (lutetium oxodotreotide Lu-177[Title/Abstract])) OR (Lutathera[Title/Abstract]))))) OR (("177Lu-octreotide, DOTA(0)-Tyr(3)-" [Supplementary Concept]) OR ((177Lu-octreotide, DOTA0, tyrosyl3-[Title/Abstract]) OR (177Lu-DOTATOC[Title/Abstract]))))) OR ((((((68Ga-DOTA-JR11[Title/Abstract]) OR (18F-AlF-NOTA-LM3[Title/Abstract])) OR (68Ga-OPS202[Title/Abstract])) OR (68Ga-NODAGA-JR11[Title/Abstract])) OR (111In-DTPA-octreotide[Title/Abstract])) OR (68Ga-DATA(5m)-LM4[Title/Abstract])))) OR (((((177Lu-DOTA-JR11[Title/Abstract]) OR (177Lu-DOTA-LM3[Title/Abstract])) OR (tetulomab tetraxetan lu-177[Title/Abstract])) OR (177LU-DOTA-HH1[Title/Abstract])) OR (177Lu-Satoreotide Tetraxetan[Title/Abstract]))))) AND ((((Theranostics[Title/Abstract]) OR (Theranostic[Title/Abstract])) OR (("Therapeutics"[Mesh]) OR (((((Therapeutic[Title/Abstract]) OR (Therapy[Title/Abstract])) OR (Therapies[Title/Abstract])) OR (Treatment[Title/Abstract])) OR (Treatments[Title/Abstract])))) OR (("Diagnosis"[Mesh]) OR ((((((((((((((Diagnoses[Title/Abstract]) OR (Diagnose[Title/Abstract])) OR (Diagnoses[Title/Abstract] AND Examinations[Title/Abstract])) OR (Diagnoses[Title/Abstract] AND Examination[Title/Abstract])) OR (Examination[Title/Abstract] AND Diagnoses[Title/Abstract])) OR (Examinations[Title/Abstract] AND Diagnoses[Title/Abstract])) OR (Antemortem Diagnosis[Title/Abstract])) OR (Antemortem Diagnoses[Title/Abstract])) OR (Diagnoses, Antemortem[Title/Abstract])) OR (Diagnosis, Antemortem[Title/Abstract])) OR (Postmortem Diagnosis[Title/Abstract])) OR (Diagnoses, Postmortem[Title/Abstract])) OR (Diagnosis, Postmortem[Title/Abstract])) OR (Postmortem Diagnoses[Title/Abstract]))))).

Participant or population Patients with suspected Neuroendocrine tumors or patients with Neuroendocrine tumors.

Intervention Radiolabeled somatostatin receptor agonists or antagonists.

Comparator Comparison of diagnostic and therapeutic effects between antagonists and agonists.

Study designs to be included RCT, or cohort study, or case-control study; Prospective research and retrospective research.

Eligibility criteria Inclusion criteria: (1) studies using radiolabeled somatostatin receptor agonists or antagonists to diagnose or treat patients with neuroendocrine tumors; (2) studies evaluating diagnostic efficacy can use histopathology and/or imaging or clinical follow-up as reference standards, and evaluate treatment efficacy by RECIST1.1 criteria to assess treatment response; (3) patient-based studies; (4) provide sufficient data for meta-analysis. Exclusion criteria: (1) reviews or meta-analyses, case reports; (2) articles providing insufficient data for meta-analysis; (3) research content is irrelevant to this study; (4) publications with overlapping study populations; (5) patients with secondary malignancies were excluded from the study.

Information sources Bibliographic databases PubMed, Cochrane, EMBASE, Ovid, Scopus, and Web of Science were searched. The search included a combination of the following terms: (1) neuroendocrine tumors; (2) “theranostics” OR “treatment” OR “diagnosis”; (3) somatostatin receptor; (4) “antagonist” OR “agonist”.

Main outcome(s) Diagnostic efficacy and treatment efficacy will be summarized.

Quality assessment / Risk of bias analysis The evaluation method depends on the final research typeDepends on the type of final analysis.

Strategy of data synthesis STATA 18 will be used for statistical calculations in this study.

Subgroup analysis If the literature is sufficient, subgroup analysis will be performed.

Sensitivity analysis If the combined results of the remaining documents are not significantly different from those without deletion, it means that the sensitivity analysis has passed.

Language restriction English.

Country(ies) involved Germany, Iran, China.

Keywords Neuroendocrine tumors; theranostics; somatostatin receptor; agonists; antagonists; meta-analysis.

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