Competition with excess of Gefitinib

The epidermal growth factor receptor (EGFR) is an established target for the treatment of advanced non-small cell lung cancer (NSCLC). TKIs targeting EGFR are standard treatment of tumors harboring EGFR mutation (ie, L858R) unfortunately, the majority of patients develop a resistance to the TKI within 1 year which is for most of them (~50%) related to an acquired T790M mutation of EGFR. TKI PET imaging can provide a diagnostic tool to determine and predict the activity of EGFR and the responsiveness to EGFR TKI. This work was partly supported by a grant from the French Government.

Rat microsomal phosphorylation activity of EGFR and the responsiveness to EGFR TKI

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Clinical diagnostic and treatment follow up of NSCLC

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CONCLUSIONS

> Within the IMakinib® program, a new TKI-PET radiotracer targeting EGFR has been developed based on the Nanocyclix technology.

> The EGFR radiotracer development was performed in collaboration with the CERRP and CEA-Cyceron academic institutions. In the mean time, the whole development flowchart, from radiochemistry to clinical PET imaging, is manageable in Pharmimage platforms for academic and industrial projects.

> In-vitro D52004436 compound showed a biochemical profile comparable to gefitinib on WT EGFR or L858R mutated EGFR whereas improved activity is observed on L858R/T790M EGFR.

> In-vivo studies suggested that the radiotracer ["[19F]-ODS2004436 binds selectively to activated EGFR, and is a good candidate to evaluate the EGFR activity by MALSCC.

> Clinical evaluation of this novel radiotracer is ongoing (First in man phase 0/I clinical trial NCT02847377).

In-vivo binding experiments showed that ["[19F]-ODS2004436 specifically bound to cell line tumor samples expressing EGFR.

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Preclinical proof of concept for the first ["[19F]-Nanocyclix® TKI-PET radiotracer targeting activated EGFR positive lung tumors

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