SATT SUD-EST
ACCELERATING TECHNOLOGY TRANSFER

THE INTERFACE BETWEEN COMPANIES AND PUBLIC RESEARCH IN SOUTH EASTERN FRANCE

TRIAZOLES & CANCER

TRIAZOLE DERIVATIVES TO FIGHT MYELODYSPLASTIC SYNDROMES AND ACUTE MYELOID LEUKEMIA

BENEFITS

- INNOVATIVE SMALL MOLECULES
- NON-APOPTOTIC CELL DEATH PATHWAY
- REDUCTION OF TUMOR GROWTH
- ACTIVE ON AZACITIDINE-RESISTANT CELL LINES

KEYWORDS

- MYELODYSPLASTIC SYNDROMES
- ACUTE MYELOID LEUKEMIA
- CHRONIC MYELOID LEUKEMIA
- TRIAZOLE DERIVATIVES
- MTOR PATHWAY

IP STATUS

- PATENT

Centre Hospitalier Universitaire de Nice
Université Nice Sophia Antipolis
Inserm
cnrs

PARTNERSHIPS

- LICENSE AND/OR
- R&D COLLABORATION (POSSIBLE CO-FUNDING)

CONTACT

licensing@sattse.com
+33 (0)4 13 24 66 10

www.sattse.com

BACKGROUND

Myelodysplastic syndromes (MDS) are estimated to occur at a rate between 4 and 5 for every 100,000 people in the world. Approximately 13,000 people in the United States and 2,500 in France are diagnosed each year.

40% of MDS patients have an innate resistance to azacitidine, the standard treatment for severe MDS, and even 100% become resistant during treatment. 33% of MDS evolve in acute myeloid leukemia (AML). The median survival of patients with AML is 4 months.

HOW IT WORKS

A scientific team demonstrated that two new classes of triazole derivatives:

- Kill cancerous cells by autophagy via the mTOR signaling pathway;
- Are active with caspase and apoptosis independent effects and did not induce cell cycle arrest;
- Demonstrate interesting *in vitro* activities on chronic myeloid leukemia (K562 cell line), acute monocytic leukemia (MOLM-13, MOLM-14, OCI-AML2, and OCI-AML3 cell lines), and myelodysplastic syndromes (SKM1-R, an azacitidine-resistant cell line, and SKM1-S).

The clinical positioning of these triazole derivatives should be on MDS patients resistant to azacitidine and/or evolving into AML.

KEY BENEFITS vs. STATE OF THE ART

Reference MDS treatments are azacitidine (Vidaza®), decitabine (Dacogen®), lenalidomide (Revlimid®) and imatinib (Gleevec®) but new therapeutic options are always required:

- A family of innovative and patentable triazole derivatives active on azacitidine resistant and sensible cell lines
- Some triazole derivatives have demonstrated superior activities (*in vitro* and *in vivo*) to the reference treatments
- Caspase and apoptosis independent cell death mechanisms should reduce the development of resistance
- Could be candidate for orphan designation

DEVELOPMENT STATUS

In vitro results: molecules of this family demonstrated *in vitro* submicromolar IC_{50} (200-900nM) on various MDS and AML cell lines,

In vivo results: other molecules of this family demonstrated *in vivo* activities (5-10 mg/kg, i.p.) in various mouse models of cancer (MDS, AML, CML...),

Ongoing lead optimization, and preclinical validation on MDS/AML mouse models.

APPLICATIONS

Myelodysplastic syndromes with resistance to azacitidine
Myelodysplastic syndromes evolving into acute myeloid leukemia
Acute myeloid leukemia and Chronic myeloid leukemia

Project financed with the support of the European Union with the European Regional Development Fund

UNION EUROPÉENNE Fonds Européen de Développement Régional
Région Provence Alpes Côte d'Azur