Pralsetinib (BLU-667) demonstrates robust activity in RET-fusion-driven intracranial tumor models

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RET kinase is oncogenic in diverse cancer subtypes

Onconogenic alterations in RET, a tyrosine kinase receptor, cause ligand-independent kinase activation across a wide range of cancers, driving tumor formation and growth. RET fusions are implicated as the underlying cause of disease in ~1-2% of patients with NSCLC. Patients with NSCLC have an estimated 5-year survival rate of 18%. Brain metastases, which portend a particularly poor prognosis, occur in about 40% of these patients.

Pralsetinib was crafted to selectively target oncogenic RET kinase

Pralsetinib selectively inhibits oncogenic RET fusions and gatekeeper mutants

Pralsetinib showed significant anti-tumor activity in KIF5b-RET fusion-driven intracranial tumors

Pralsetinib demonstrated anti-tumor activity and strong target engagement in an intracranial CCDC6-RET-driven tumor model

Pralsetinib was active against intracranial metastases in the clinical setting

Pralsetinib is being evaluated in a clinical trial for patients with RET-altered tumors

CONCLUSIONS

- Pralsetinib has broad anti-tumor activity in intracranial tumor models regardless of RET-fusion partner
- Pralsetinib showed broad, durable anti-tumor activity in patients with RET-fusion NSCLC, both systemically and in the brain
- ARROW clinical trial enrollment continues in treatment naïve RET-fusion-positive NSCLC (NCT03037385)

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References

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