**Background & objective**

Bemcentinib is being developed as monotherapy and in combination with immune-, targeted, and chemo-, therapy in NSCLC, AML/MDS and melanoma.

### Key inclusion criteria
- Patients with AML who are not suitable for intensive chemotherapy as a result of advanced age or comorbidities and who are suitable to receive treatment with cytarabine or decitabine
- Patients with AML who are candidates for allogenic BM transplantation
- Patients with a matched donor
- Eastern Cooperative Oncology Group (ECOG) performance status 0, 1 or 2
- Patients with non-refractory Myelodysplastic Syndrome (MDS) who are not suitable for intensive therapy
- Patients with AML who are not suitable for intensive chemotherapy as a result of advanced age or comorbidities and who are suitable to receive treatment with cytarabine or decitabine
- Patients with advanced NSCLC whose disease is refractory to first-line chemotherapy and who have progressed on at least one prior line of chemotherapy

### Key exclusion criteria
- Patients with prior treatment with any other BTK, BCL2, or BCR-ABL kinase inhibitors
- Patients with prior treatment with any other anti-CD47 antibodies
- Patients with prior treatment with any other immuno-oncology agents
- Patients with prior treatment with any other AXL kinase inhibitors

### Additional criteria
- AML: Patients with AML who are not suitable for intensive chemotherapy as a result of advanced age or comorbidities and who are suitable to receive treatment with cytarabine or decitabine
- NSCLC: Patients with non-refractory NSCLC whose disease is refractory to first-line chemotherapy and who have progressed on at least one prior line of chemotherapy
- MDS: Patients with non-refractory MDS who are not suitable for intensive therapy

### Study rationale
- AXL is a receptor tyrosine kinase expressed on tumour and immune cells and a member of the TAM family (Tyro-AXL-Mer) of kinases.
- AXL is overexpressed in response to a hostile tumour microenvironment and drives a tumour survival programme resulting in resistance to chemotherapy, radiotherapy and immune checkpoint inhibitors.
- AXL is overexpressed in up to 30% of AML cases and is a negative prognostic factor for AML. It is a Validated target for AML, and novel inhibitors of AXL have shown promising preclinical and clinical activity.

### Bencentinib
- Bemcentinib is a selective AXL kinase inhibitor.
- It potentiates the effects of chemotherapy and immune checkpoint inhibitors in preclinical models.
- It shows promising clinical activity in a phase 1 trial.

### Clinical Trial: A Phase 2 clinical trial of selective AXL inhibitor bemcentinib and low dose cytarabine (LDAC) or decitabine

<table>
<thead>
<tr>
<th>Disease Status</th>
<th>LDAC + Bemcentinib</th>
<th>Decitabine + Bemcentinib</th>
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<tbody>
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<td>First-Line</td>
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<td>Relapsed</td>
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<td>Refractory</td>
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<td>Secondary</td>
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### Efficacy - durable survival

**Responses in evaluable patients**

- **ORR:** 25% (3/12) (4 CR/CRi + 2 PR)
- **Median duration of response:** 14 months (4 CR/CRi + 2 PR)
- **3-year overall survival:** 50% (4 CR/CRi + 2 PR)

### Adverse Events

**Any event, n (%)**

- **LDAC + Bemcentinib:** 13 (81%) 12 (75%)
- **Decitabine + Bemcentinib:** 15 (88%) 14 (82%)

- **AEs in Dose Escalation phase:** 9 (53%) 4 (24%)
- **AEs in Cohort expansion phase:** 4 (24%) 1 (6%)
- **Electrocardiogram QT prolonged:** 3 (19%) 2 (13%)
- **Diarrhoea:** 4 (24%) 1 (6%)
- **Diabetes:** 1 (6%) 2 (12%)
- **Hypersensitivity:** 1 (6%) 0
- **Peripheral oedema:** 3 (18%) 0

### Conclusions

The LDAC+bemcentinib combination showed significant promising efficacy among elderly AML patient population with 80% aged >75 years both in first-line unselected newly diagnosed AML patients and as 2nd/3rd line in relapsed AML patients.

Bemcentinib appears relatively safe and well tolerated in combination with both LDAC and decitabine.

The ORR, seen particularly in combination with LDAC and cytarabine, is significantly higher than previously observed/historical benchmarks in single-agent cytarabine.

Further testing in late-stage trials is warranted.