CONCLUSIONS

- In patients with sarcoma, mipasematamuzotin (Mipa) monotherapy demonstrated an acceptable safety profile and antitumor activity, with tumor shrinkage, tumor volume reduction, and achievement of a partial response at week 12 during dose-escalation.

- Smaller increases in concentration between corollary antibody (HA) and total AXL demonstrate good in vivo stability of the antibody-drug conjugate (ADC) rapid disposition indicates no accumulation with 1 cycle of treatment.

- Although the non-dosed area (NDA) has not been reached and the maximum tolerated dose (MTD) has not been reached due to the prohibitory efficacy and evidence of treatment-emergent adverse events (TEAEs) Mipa 15 mg is the highest and last dose explored in a fixed-dose every 3 q4w regimen.

- AXL, galectin-3, and PD-L1 expression in solid tumors with sarcoma, characterized by measured tissue intensity (HTC), with 56% of patients showing AXL positive tumors, the 2 remaining patients have intermediate levels of expression.

- The study continues to enroll patients to further optimize the Mipa monotherapy dosing regimen and continue to evaluate Mipa in combination with pembrolizumab.

INTRODUCTION

- AXL is a cell surface receptor tyrosine kinase widely expressed in solid tumors, including sarcomas.

- AXL overexpression is linked to increased metastatic potential, chemotherapy resistance, and worse overall survival in some solid tumors, notably sarcoma and non-small cell lung cancer (NSCLC).

- ADC-601 (mipasematamuzotin), an ADC comprising a humanized anti-AXL antibody conjugated via a Vicarbicidin linker to the potent chemotherapeutic SG1199 (poribendamebolome) derivate oligopyrimidine.


OBJECTIVE

- To characterize the safety and tolerability of Mipa in patients with selected sarcoma indications who have exhausted standard of care therapy.

METHODS

Study Design

- This is a phase 1/2, open-label, dose-escalation (part 1), dose-expansion (part 2) study of Mipa (KET01830402, EudraCT:2021-00565-18) (Figure 1).

- Part 1: Patients with sarcoma who have AXL gene amplification, patients with sarcoma, or patients with NSCLC received escalating doses of Mipa monotherapy Q2W until disease progression or unacceptable toxicity.

- A 3 + 3 dose-escalation design.

- In part 2, patients will receive the recommended dosing regimen for expansion determined in part 1 or an alternative dosing regimen.

Outcomes

- The primary endpoints are the Frequency and severity of adverse events and serious adverse events; the incidence of dose-limiting toxicity (DLT) dose escalation; the frequency of interstitial edema or dose reductions; and the changes from baseline in laboratory safety values, vital signs, ECG performance status, and 12 lead electrocardiograms.

- Secondary endpoints include overall response rate (ORR) 1), duration of response, progression-free survival, overall survival, pharmacokinetics (PK), and antitumor activity response.

Eligibility Criteria

Table 1 Key inclusion and exclusion criteria

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<thead>
<tr>
<th>Key Inclusion Criteria</th>
<th>Key Exclusion Criteria</th>
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<tr>
<td>Adult (18 years of age)</td>
<td>Ineligibility due to severe comorbidities or risk factors.</td>
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<td>Pathological diagnosis of locally advanced or metastatic solid tumor malignancy</td>
<td>Uncontrolled intercurrent illness or psychiatric illness that would make the patient unsuitable for study.</td>
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<td>Particular histology of NSCLC, regardless of age and performance status</td>
<td>Current or history of prior radiotherapy, chemotherapy, or immunotherapy.</td>
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<td>Measurable disease RECIST 1.1 (soft and/or hard tissue lesions)</td>
<td>History of another investigational product in the previous 28 days.</td>
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<tr>
<td>ECOG performance status 0-2</td>
<td>Previous radiotherapy, chemotherapy, or immunotherapy.</td>
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<tr>
<td>Adequate organ function</td>
<td>Significant medical comorbidity.</td>
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<tr>
<td>Previous 4+ ATRK, cancer signal</td>
<td>History of a prior anticancer regimen.</td>
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RESULTS

Patient Population

- As of February 6, 2024, 24 patients with sarcoma, unevaluated for AXL expression, were enrolled in 4 different dose cohorts to be treated with Mipa 7.5 mg, 11 mg, and 15 mg Q2W.

- Disease progression occurred in 1 patient treated with Mipa 11 mg Q2W and 1 patient treated with Mipa 15 mg Q2W.

Pharmacokinetics

- PK data were available from 19 patients in cycle 1 and 17 patients in cycle 2.

- Mipa mean exposure tended to increase with dose. Mipa mean exposure demonstrated notable inter-subject variability rapid disposition, and no accumulation over cycle 2 (Figure 4).

- Low levels of metabolic pathways and high variability of SG1199 preserved its characteristic for most patients.

AXL Expression by IHC in Sarcoma Baseline Biopsies

- AXL-positive T1Cs were present in all sarcoma baseline biopsies tested to date (13 sarcomas).

- Of 14 patient baseline patients, 2 patients showed positive co-axial tumor cells.

- The 2 responding patients (PR) showed intermediate levels of AXL expression by IHC (baseline positive T1Cs and staining intensity). (Figure 5).

- AXL IHC expression in TSCs of sarcoma baseline biopsies (A+) and intermediate AXL IHC-negative levels in patients with a PR (B)