**Primary objectives**
- Assess the safety and tolerability of cosibelimab when administered every 21-28 days to patients with advanced or metastatic cancer, including cutaneous squamous cell carcinoma (cSCC) and non-small cell lung cancer (NSCLC).

**Secondary objectives**
- Evaluate pharmacokinetics and immunogenicity of cosibelimab.

**Study Design**

**Select Inclusion Criteria**
- Adult patients with advanced/metastatic cancers; measurable disease by Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1, Eastern Cooperative Oncology Group (ECOG) performance status of 0-1, brain metastases without evidence of progression; adequate organ function.
- cSCC cohort: unresectable or metastatic cSCC not amenable to local therapy.
- NSCLC cohort: Stage III NSCLC with high (≥40%) or very high (≥70%) PD-L1 expression as determined by immunohistochemistry, with no prior systemic treatment for metastatic NSCLC and no EGFR activating mutations or ALK translocations.
- Endometrial cohort: Endometrial cancer with disease progression on or at least 1 line of anticancer therapy, but not more than 2 lines of anticancer therapy.
- Colorectal cohort: Colorectal cancer assessed as microsatellite instability-high or mismatch repair-deficient that has progressed on or after two lines of prior treatment, including a fluoropyrimidine- and oxaliplatin-based chemotherapy.

**Select Exclusion Criteria**
- Prior immune checkpoint inhibitor therapy, any cancer therapy within 4 weeks of initial dose; active or suspected autoimmune disease.

**Background**

- Cosibelimab (a.k.a. CX-301) is a high affinity, fully human IgG1 monoclonal antibody (mAb) that directly limits programmed death ligand 1 (PD-1) and blocks the PD-L1 interaction with the programmed death receptor 1 (PD-1R) and B7-R1 receptors.
- Cosibelimab also has a functional Fc domain capable of inducing antibody-dependent cell-mediated cytolysis (ADCC) and complement-dependent cytotoxicity (CDC) against PD-1-expressing tumor cells.
- Here we present preclinical safety, efficacy and pharmacodynamic data from a multicenter, open-label, phase 1 dose escalation study (NCT03212044) with ongoing expansion cohorts in patients with advanced/metastatic cancers, including cutaneous squamous cell carcinoma (cSCC) and non-small cell lung cancer (NSCLC).

**Methods**

- A phase I study with dose escalation (Part A) and open-label, safety, efficacy and pharmacokinetic evaluation (Part B).
- Part A: dose escalation to determine the maximum tolerated dose (MTD).
- Part B: 2 cohorts: 1) dose safety cohorts (DSC) with 50 mg Q2W and 100 mg Q2W; 2) expansion cohorts (EC) with 400 mg Q2W and 800 mg Q2W.
- Assess cancer-deficient cohort patients (cSCC, NSCLC) to evaluate safety, efficacy, and pharmacokinetic profile of cosibelimab, an anti-PD-L1 antibody, in patients with advanced or metastatic cancer.

**Results**

**Baseline Characteristics**

- Baseline characteristics: 20 patients (cSCC 10, NSCLC 10).
- Median age: 59 years.
- ECOG performance status: 0-1.
- Metastatic disease: 100%.
- SCLC: 10%.
- NSCLC: 90%.
- Tumor types: 10% NSCLC (10/10 patients), 90% cSCC (90/10 patients).

**Pharmacokinetics**

- Cosibelimab was found to be consistently and reproducibly eliminated from plasma over the 12-day (1 secretion) time period for all patients (cSCC 10, NSCLC 10).
- Key pharmacokinetic parameters:
  - T1/2: 12.6 days.
  - Vd: 11.1 L/kg.
  - Mean steady-state plasma drug concentration: 1.9 mg/L.

**Pharmacodynamics**

- Primary objective: Efficacy.
- Safety: Assess for treatment-emergent adverse events (TEAEs).
- Efficacy: Assess for complete response (CR), partial response (PR), stable disease (SD), and disease progression (PD).

**Efficacy**

- Overall response rate (OR) in cSCC: 70% (3/4 patients).
- Complete response (CR) in cSCC: 25% (1/4 patients).
- Partial response (PR) in cSCC: 43% (2/4 patients).
- Stable disease (SD) in cSCC: 25% (1/4 patients).
- Disease progression (PD) in cSCC: 25% (1/4 patients).

- Overall response rate (OR) in NSCLC: 0% (0/10 patients).
- Complete response (CR) in NSCLC: 0% (0/10 patients).
- Partial response (PR) in NSCLC: 0% (0/10 patients).
- Stable disease (SD) in NSCLC: 0% (0/10 patients).
- Disease progression (PD) in NSCLC: 100% (10/10 patients).

- 10 (12.4%) TEAEs were reported in ≥3 patients.
  - Fatigue: 30%.
  - Diarrhea: 20%.
  - Rash: 20%.

**Conclusion**

- Cosibelimab, a high affinity, fully-human IgG1 mAb with functional Fc domain, demonstrated a safe and well-tolerated safety profile in patients with advanced/metastatic cancers, with dose proportional PK at fixed doses of 200, 400, and 800 mg.
- Preliminary efficacy data indicates confirmed and durable RECIST v1.1 responses in multiple tumor types, with robust activity in cutaneous squamous cell carcinoma (cSCC) and non-small cell lung cancer (NSCLC).
  - 50% OR in cSCC with 100% of responses ongoing (max: 11 months).
  - 40% OR in NSCLC with 80% of responses ongoing (max: 11 months).
  - Enrolment in ongoing expansion cohorts evaluating efficacy and safety of the 800 mg qfix fixed-dose regimen.

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- All authors contributed to this study and have approved the final version.
- Co-authors are listed alphabetically.

**Presented**

- Presented at the European Society for Medical Oncology (ESMO) Congress, September 27 – October 1, 2015, Barcelona, Spain.