IKS014: HER2-directed ADC for solid tumors

TARGET: HER2

ANTIBODY: Anti-HER2 monoclonal IgG1, humanized

LINKER: Site-specific conjugation of β-glucuronide for tumour-selective enzymatic payload activation and release

DRUG/PAYLOAD: Auristatin MMAF

DRUG DESCRIPTION: IKS014 is a class-leading ADC that incorporates an anti-HER2 antibody conjugated to the tubulin polymerization inhibitor MMAF via site-specific conjugation, with tumour-selective payload activation and release via glucuronide linker formats.

CLINICAL STUDIES: Class leading clinical profile.

Phase 1a: 70 evaluable patients with advanced HER2+ cancers who failed on previous HER2 therapies. Median number of prior therapies was 4

Recommended Dose for Dose Expansion: 105 mg/m^2 (2.8mg/kg) once every 3 weeks

At a median follow-up of 6.6 months (Data cut-off 31 07 25, n = 62):

Efficacy

- ORR: Breast cancer; 64% (at doses ≥ 90 mg/m^2)
  Oesophageal cancer: 50%

Safety

- No ILD at any grade; G1/ G2 pneumonitis only
- No ocular (corneal) DLTs; G1/ G2 keratitis (low frequency)
- Low incidence of neutropenias
- No thrombocytopenia
- Sig reduced GHI toxicities compared with other HER2-directed ADCs (Enhertu, Kadcyla)

PRECLINICAL STUDIES: Best-in-class efficacy (MED in mouse xenograft and PDX models); **Best-in-class safety** (HNSTD NHPs); Preclinical TI is significantly superior to in-clinic and on-market HER2-directed ADCs.

Efficacy: Significantly enhanced efficacy over Kadcyla; similar or better efficacy than Enhertu. In JIMT-1 (HER2 2+ BC), IKS014 induced complete regression with 5mg/kg single dose; Enhertu shows marginal regression at 10mg/kg. IKS014 is active in Kadcyla-resistant HER2+ gastric cancer models. **Safety:** GLP toxicology; HNSTD >12mg/kg (single dose) with no ocular or ILD-related toxicities. Preclinical TI is >4-fold higher than Enhertu and >10-fold higher than Kadcyla.

DEVELOPMENT STATUS: Phase 1b (Iksuda WW trial); Phase 3 (Fosun Pharma, in China as FS-1502)

CLINICAL INDICATION: HER2+ advanced solid tumours:

- Breast cancer (BC)
- Gastric (GC), gastro-oesophageal-junction (GEJ), oesophageal cancers
- Other HER2+ solid tumours and HER2-mutated lung cancer

CLINICAL TRIALS

IKS014 in advanced solid tumors that express HER2
NCT05872295
https://classic.clinicaltrials.gov/ct2/show/NCT05872295
The study consists of 2 parts: dose-escalation (Part 1) and dose-expansion (Part 2).

- Estimated enrolment: 165 patients
- Enrolment sites: Australia, NZ, Singapore, US

Phase 1 Study of FS-1502 in patients with HER2 expressed advanced solid tumors and breast cancer.
NCT03944499
https://classic.clinicaltrials.gov/ct2/show/NCT03944499

- Estimated enrolment: 297 patients
- Enrolment sites: China

FS-1502 Versus T-DM1 for HER2-Positive Unresectable Locally Advanced or Metastatic Breast Cancer
NCT05755048
https://classic.clinicaltrials.gov/ct2/show/NCT05755048

- Estimated enrolment: 314 patients

PARTNERING STATUS

Available for license: WW excluding China.

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