A multicenter, randomized, double-blind, Phase 2/3 study of ficerafusp alfa (BCA101) or placebo in combination with pembrolizumab for first-line treatment of HPV-negative, PD-L1–positive, recurrent or metastatic head and neck squamous cell carcinoma: FORTIFI-HN01

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KEY TAKEAWAYS

- Human papillomavirus (HPV)-negative head and neck squamous cell carcinoma (HNSCC) is an aggressive disease characterized by epithelial growth factor receptor (EGFR) overexpression and poor immune cell tumor penetration, driven by high transforming growth factor-β (TGF-β) levels that promote a fibrotic tumor microenvironment (TME)[1-4]
- Ficerafusp alfa, a bifunctional EGFR-directed antibody combined with a TGF-β ligand trap, was designed to drive tumor penetration and provide antitumor effects within the TME and directly against cancer cells[5,6]
- In a Phase 1b study, ficerafusp alfa plus pembrolizumab treatment resulted in deep and durable responses and clinically meaningful progression-free survival (PFS) and overall survival (OS) in patients with HPV-negative, recurrent or metastatic (R/M) HNSCC, along with increased tumor penetration by immune cells[7,8]
- FORTIFI-HN01 (NCT06788990) is a Phase 2/3 study designed to investigate whether first-line (1L) treatment with ficerafusp alfa plus pembrolizumab improves objective response rate (ORR) and OS vs pembrolizumab alone in patients with HPV-negative, PD-L1–positive, R/M HNSCC

FORTIFI-HN01 STUDY STATUS

- FORTIFI-HN01 is open to enrollment at sites in North America, South America, Europe, Asia, and Oceania
- The Phase 2 portion is complete
- The Phase 3 portion is now enrolling with the optimal biological dose of ficerafusp alfa 1500 mg weekly in combination with pembrolizumab

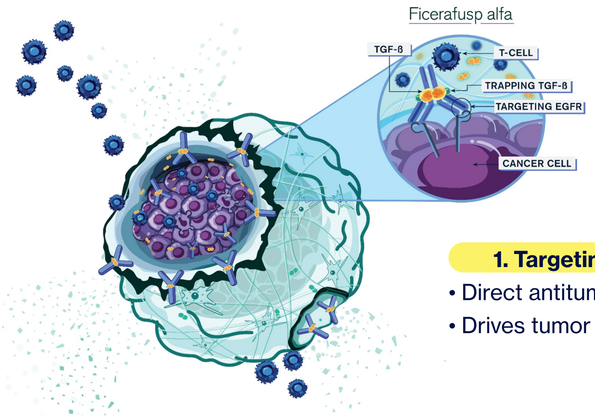
ClinicalTrials.gov

FORTIFI-HN01 clinical trial website

BACKGROUND

- Inadequate tumor penetration by immune cells and anticancer drugs into the TME is a challenge to effective treatment in various solid tumors, including R/M HNSCC[1-4]
- HPV-negative HNSCC is an aggressive disease characterized by EGFR-expressing tumor cells and high levels of TGF-β that drive a dense stromal network, resulting in immune cell exclusion and suppression, resistance to standard treatments, and a poor prognosis[2-4]
- Ficerafusp alfa is a first-in-class bifunctional antibody designed to enable tumor penetration by inhibiting both EGFR and TGF-β in the TME[5,6]

FICERAFUSP ALFA MECHANISM OF ACTION



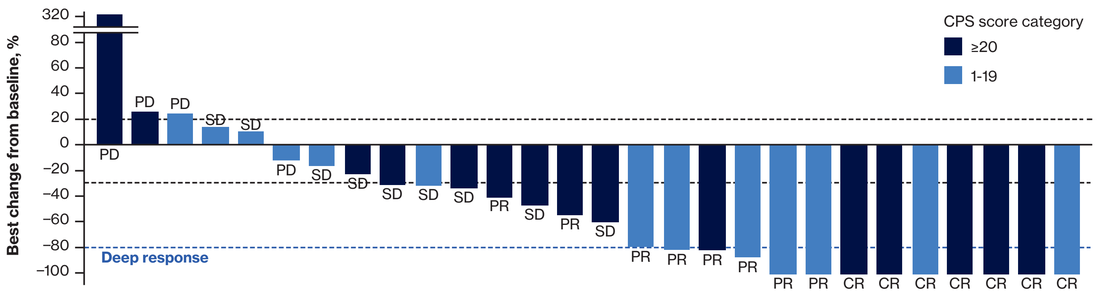
Anti-EGFR × TGF-β trap bifunctional antibody[5,6]

1. Targeting EGFR
- Direct antitumor effect
- Drives tumor targeting

2. Trapping TGF-β
- Enables tumor penetration
- Prevents resistance

PHASE 1B RESULTS

- The safety and efficacy of 1L ficerafusp alfa in combination with pembrolizumab in PD-L1 combined positive score (CPS) ≥1, R/M HPV-negative HNSCC has been evaluated in an ongoing phase 1/1b study[7,8]
  - In 28 efficacy-evaluable patients with HPV-negative disease, the confirmed ORR was 54% (CPS 1-19, 54%; CPS ≥20, 53%), including complete response (CR) in 25% of patients, and median duration of response was 21.7 months[9]
  - Median PFS was 9.9 months and median OS was 21.3 months[9]



- Two other posters describing 3-year follow-up (Abstract 6040, Poster Board 497) and exploratory analyses of depth of response (Abstract 6058, Poster Board 515) from the Phase 1b study are presented concurrently in this session[9,10]

Investigator-assessed best overall response per RECIST 1.1. One CR was detected via FDG-PET scan.
PD, progressive disease; **PR**, partial response; **SD**, stable disease.

FORTIFI-HN01 STUDY DESIGN

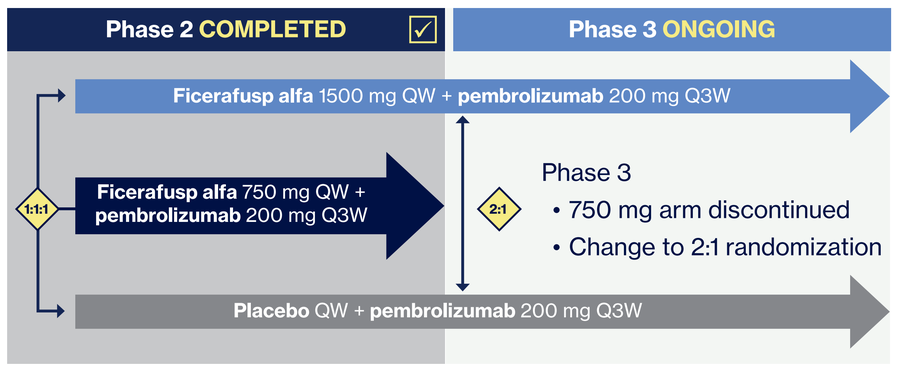
Global, multicenter, randomized, placebo-controlled, double-blind, Phase 2/3 study

FORTIFI

Population (N≈650)
- 1L R/M HNSCC excluding HPV-positive OPSCC
- CPS ≥1

Stratification factors
- PD-L1 status
- Disease extent

NCT06788990



Study treatment is administered until discontinuation, PD, or other criteria occur. Following the decision on the optimal biologic dose (Phase 2), patients randomized to the 750 mg arm crossed over to the 1500 mg arm.
OPSCC, oropharyngeal squamous cell carcinoma; **Q3W**, every 3 weeks; **QW**, weekly.

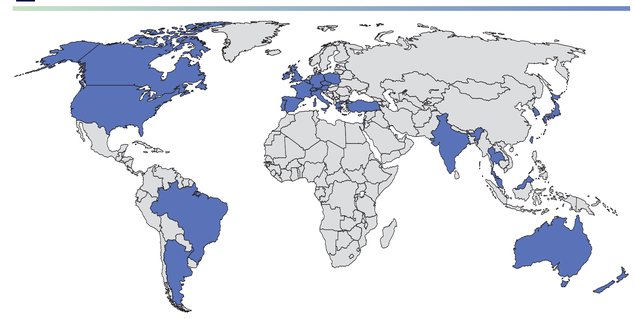
KEY ELIGIBILITY CRITERIA

Key inclusion criteria
Histologically or cytologically confirmed R/M HNSCC
Eligible primary tumor locations: oral cavity, hypopharynx, larynx, or oropharynx (HPV negative if OPSCC)
PD-L1 CPS ≥1
Measurable disease per RECIST 1.1
No prior systemic therapy for R/M disease, and completed systemic therapy >6 months prior if part of multimodal treatment for locoregionally advanced disease
Eastern Cooperative Oncology Group performance status 0 or 1
Age ≥18 years
Key exclusion criteria
Disease suitable for local therapy administered with curative intent
Prior treatment with therapy targeted to TGF-β
Prior therapy with an anti-EGFR antibody (except radiosensitizing and multimodal treatment for locoregionally advanced disease)
Prior neoadjuvant and/or adjuvant immune checkpoint inhibitor therapy completed ≤6 months prior to study treatment initiation
History of grade ≥2 intolerance or hypersensitivity reaction to anti-EGFR therapy or other murine proteins
Patients at higher risk of bleeding (including known bleeding diathesis), with current active major bleeding, or major bleeding episode ≤4 weeks prior to enrollment

ENDPOINTS

Primary endpoints
Phase 2: Safety and efficacy of the two doses to support selection of optimal biological dose
Phase 3: ORR (interim analysis) and OS (final analysis)
Secondary endpoints
Safety
Additional efficacy endpoints (including PFS, duration of response, and clinical benefit rate)
Patient-reported outcomes
Exploratory endpoint
Biomarker evaluation

STUDY LOCATIONS



Active and planned

PLAIN LANGUAGE SUMMARY

- FORTIFI-HN01 is a clinical trial for people with head and neck squamous cell carcinoma (HNSCC) that has either returned (recurrent) or spread to other parts of the body (metastatic). HNSCC develops because of mutations in cells lining the surfaces within the head and neck region, including the mouth, throat, or voice box
- The FORTIFI-HN01 clinical trial is investigating an experimental treatment called ficerafusp alfa, which targets two different proteins thought to contribute to tumor growth. It is hoped that giving ficerafusp alfa together with pembrolizumab, an approved drug for HNSCC, will be more effective than pembrolizumab treatment alone
- In the FORTIFI-HN01 clinical trial, all participants are treated with pembrolizumab. Two out of every three participants also receive ficerafusp alfa, and one out of every three participants also receive a placebo (a fake treatment with no active ingredient, used for comparison)
- It is planned that about 650 people will take part in this trial. People who have not received any treatment since their disease returned or spread to other parts of the body are allowed to participate

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