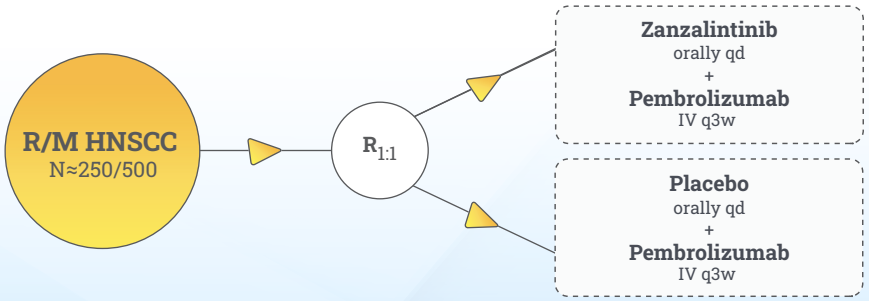
STELLAR 305

PHASE • 2/3

Phase 2/3 Study of Zanzalintinib (XL092) With Pembrolizumab vs Pembrolizumab in Recurrent or Metastatic Head and Neck Squamous Cell Carcinoma

THE COMBINATION OF ZANZALINTINIB AND PEMBROLIZUMAB
IS NOT APPROVED FOR THE USE UNDER INVESTIGATION IN THIS TRIAL.
SAFETY AND EFFICACY HAVE NOT BEEN ESTABLISHED.

A Phase 2/3, Randomized, Double-Blind, Controlled Study of Zanzalintinib in Combination With Pembrolizumab vs Pembrolizumab in the First-Line Treatment of Subjects With PD-L1 Positive, Recurrent or Metastatic Head and Neck Squamous Cell Carcinoma



Study Overview

In the phase 2 portion of the study, approximately 250 eligible patients with PD-L1 positive, R/M HNSCC will be randomly assigned to zanzalintinib in combination with pembrolizumab or pembrolizumab alone to evaluate the activity of the combination therapy on PFS by BIRC and OS vs pembrolizumab monotherapy. If phase 2 results support study continuation to phase 3, an additional 250 patients will be randomized for a total of 500 patients.

Investigational Treatment

Eligible patients will be randomly assigned in a 1:1 ratio to the following treatment arms:

- **Experimental arm:** oral zanzalintinib qd + pembrolizumab infusion q3w
- **Control arm:** oral zanzalintinib-matched placebo qd + pembrolizumab infusion q3w

Key Eligibility Criteria

- R/M HNSCC of the oropharynx, oral cavity, hypopharynx, and larynx incurable by local therapy; nasopharynx not allowed
- Measurable disease
- No prior systemic therapy for R/M HNSCC
  - Systemic therapy given as part of multimodal treatment for locally advanced disease allowed if completed >6 months prior to randomization
- PD-L1 CPS ≥1
- No prior therapy with any anti–PD-1/PD-L1/PD-L2 agent, or an agent directed to another stimulatory or co-inhibitory T-cell receptor
- No prior treatment with zanzalintinib

Key Endpoints

Multiple Primary Endpoints

- PFS by BIRC
- OS

Exploratory Endpoint

- HRQoL by EORTC QLQ-C30/ QLQ-H&N35 and EQ-5D-5L

Secondary Endpoints

- PFS by investigator
- ORR and DOR by BIRC and investigator

Participating Regions

Approximately 200 sites globally in

- North America
- South America
- Europe
- Asia Pacific

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For more information, please contact

Principal Investigator: _____

Study Coordinator: _____

Contact Number: _____

Site Address: _____

Email: _____

To learn more about this trial, visit clinicaltrials.gov and search for **NCT06082167**.

BIRC, blinded independent radiology committee; **CPS,** combined positive score; **DOR,** duration of response; **EORTC QLQ-C30/QLQ-H&N35,** European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire—Core 30/Head and Neck 35; **EQ-5D-5L,** EuroQoL health questionnaire instrument; **HNSCC,** head and neck squamous cell carcinoma; **HRQoL,** health-related quality of life; **IV,** intravenous; **ORR,** objective response rate; **OS,** overall survival; **PD-1,** programmed death receptor-1; **PD-L1,** programmed death receptor-1 ligand; **PD-L2,** programmed death receptor-2 ligand; **PFS,** progression-free survival; **q3w,** once every 3 weeks; **qd,** once daily; **R,** randomization; **R/M,** recurrent or metastatic.

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