Phase 2 study of oral CCR4 antagonist FLX475 (tivumecirnon) plus pembrolizumab in subjects with head and neck squamous cell carcinoma (HNSCC) previously treated with checkpoint inhibitor

**ABSTRACT**

**INTRODUCTION**

• FLX475 (Tivumecirnon, or TIVU) is a selective CCR4 antagonist designed to block the recruitment of immunosuppressive regulatory T cells (T_{reg}) into the tumor microenvironment. The FLX475-02 trial (NCT04374167) is a phase 2 study of FLX475 as monotherapy and in combination with pembrolizumab in subjects with advanced cancer. Early encouraging data on the biological effects, safety and antitumor activity of FLX475 have previously been presented.1 We now present the results from the Phase 2 cohort of combination therapy in subjects with head and neck squamous cell carcinoma (HNSCC) previously treated with checkpoint inhibitor (CPI)-experienced.

**METHODS**

Subjects with CPI-experienced, recurrent or metastatic (R/M) HNSCC received FLX475 100 mg orally once daily with pembrolizumab (200 mg IV Q3 weeks). The primary study objectives were safety and tolerability, and antitumor activity. The primary efficacy endpoint was overall response rate (ORR), based on RECIST 1.1 criteria. Additional efficacy endpoints included progression-free survival (PFS). Safety was evaluated as per CTCAE v4.03. Data cutoff was 04Mar22.

**RESULTS**

- **Demographics**
  - Median age: 65 years (range 28-83)
  - Median Eastern Cooperative Oncology Group (ECOG) performance status: 0

- **Combination vs. pembrolizumab**
  - Combination arm included 22 subjects received TIVU 100 mg orally once daily with pembrolizumab 200 mg IV Q3 weeks.
  - Pembrolizumab monotherapy arm included 18 subjects.

- **Endpoints**
  - **Progression-Free Survival (PFS)**
    - Median PFS in the combination arm was 5 months (range 2.2-40.1) and median lines of prior therapy were 3 (1-6).
  - **Objective Response Rate (ORR)**
    - FLX475 pembrolizumab combination therapy in subjects with head and neck squamous cell carcinoma (HNSCC) previously treated with checkpoint inhibitor (CPI)-experienced.
  - **Median duration of treatment** of 19.6 months in subjects with HNSCC.

**CONCLUSIONS**

- FLX475 in combination with pembrolizumab was well tolerated and showed encouraging clinical activity including in those with HPV-positive tumors, supporting the continued development of this combination therapy for CPI-experienced HNSCC.

**REFERENCES**


**ACKNOWLEDGMENTS**

This study was sponsored by RAPT Therapeutics, Inc.

**CONCLUSIONS**

- In this completed Phase 2 cohort of subjects with CPI-experienced R/M HNSCC, FLX475 (TIVU)/pembrolizumab was well tolerated and showed encouraging clinical activity including in those with HPV-positive tumors.
- 68% subjects received ≥ 3 prior lines of treatment (up to 6)
- Confirmed ORR 15.6% (5/32) in all and 22.2% (4/18) HPV+ subjects
- Median duration of treatment of 19.6 months in subjects with HNSCC.
- These data support the continued development of TIVU plus checkpoint inhibitor combination therapy for CPI-experienced HNSCC.

**REFERENCES & DISCLOSURES**


**ACKNOWLEDGMENTS**

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