Updated dose expansion results of a Phase 1/1b study of the bifunctional EGFR/TGFβ inhibitor BCA101 with pembrolizumab in patients with recurrent, metastatic head and neck squamous cell carcinoma

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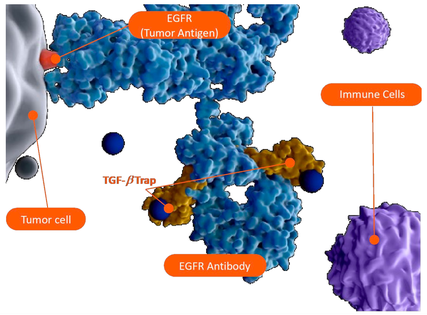
INTRODUCTION

Proposed mechanisms of action of BCA101:

- Localizes TGFβ inhibition to the TME through an EGFR-directed approach
- Aims to increase anti-tumor activity via enhanced ADCC and increased NK cell activation
- TGFβ inhibition prevents a mesenchymal phenotype to allow EGFR inhibition to continue to work and prevent resistance



METHODS

Simon-2-stage design n=39 evaluable (stage 1/2, n=18+21)

Study treatment

BCA101 (anti-EGFR/TGFβ-trap) 1500mg qw in combination with pembrolizumab 200mg q3w.

Key Inclusion Criteria:

- HNSCC, metastatic or unresectable, recurrent with a PD-L1 Combined Positive Score (CPS) ≥1.
  Note: CPS determined locally using 22C3 IHC or other validated assay.
- Primary tumor locations: oropharynx, oral cavity, hypopharynx, or larynx.
- No prior systemic therapy administered in the R/M setting (exception: completed >6 months prior if given as part of multimodal treatment for locoregionally advanced disease).
- No prior immune checkpoint inhibitors (exception: neoadjuvant therapy >6 months prior).
- No prior history of anti-EGFR antibodies (exception: radiosensitizing agents and multimodal treatment for locally advanced disease).
- HPV testing by p16 IHC for oropharyngeal cancer.

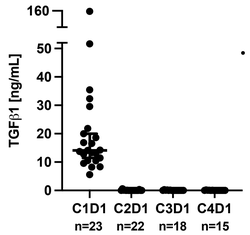
RESULTS

Baseline Characteristics

Table 1	Safety Set	N = 42 (100%)
Age	Median (range)	63 (31-84)
Sex – n (%)	Male/Female	30/12 (71% vs. 29%)
HNSCC Primary site of disease	Oropharynx	20 (48%)
	HPV-pos	12 (60% of Oropharynx)
	HPV-neg	8 (40% of Oropharynx)
	Oral Cavity	14 (33%)
	Hypopharynx	4 (10%)
	Larynx	4 (10%)
CPS - n (%)	1-19	22 (52%)
	≥20	20 (48%)
Locoregional vs. distant metastatic	LR only	11 (26%)
	LR + DM	16 (38%)
	DM only	15 (36%)
ECOG 0 vs.1 (%)		19 vs. 23 (45% vs. 55%)

Pharmacodynamics

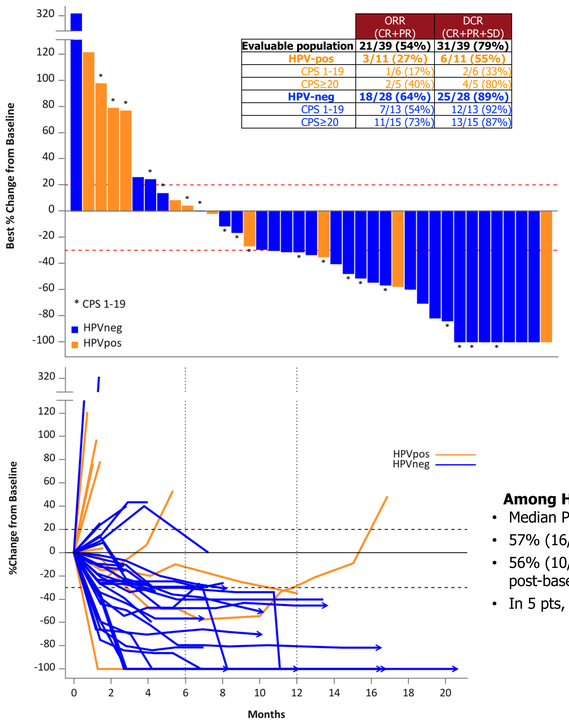
Figure 1: TGFβ1 concentration in plasma



- Full neutralization of TGFβ1 in plasma in patients treated with BCA101 + pembrolizumab

Efficacy

Figure 2: Anti-tumor activity of BCA101 in combination with pembrolizumab



Evaluable population	ORR (CR+PR)	DCR (CR+PR+SD)
HPV-pos	3/11 (27%)	6/11 (55%)
CPS 1-19	1/6 (17%)	2/6 (33%)
CPS≥20	2/5 (40%)	4/5 (80%)
HPV-neg	18/28 (64%)	25/28 (89%)
CPS 1-19	7/13 (54%)	12/13 (92%)
CPS≥20	11/15 (73%)	13/15 (87%)

ORR in HPV-neg (n=28 evaluable)

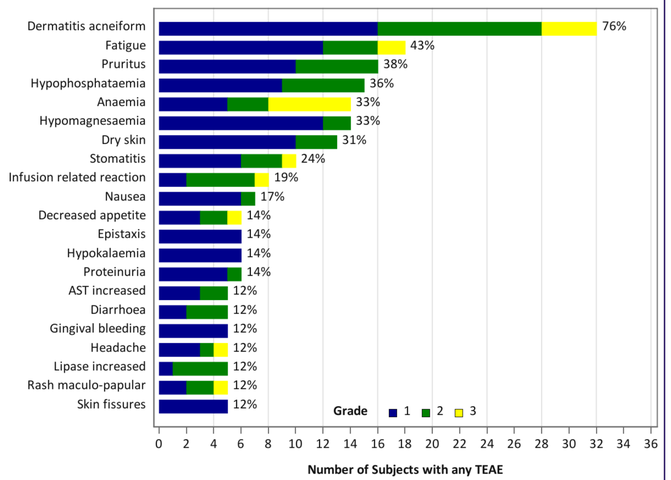
- **By CPS**
  - CPS 1-19 (54%, 7/13)
  - CPS≥20 (73%, 11/15)
- **By site of disease:**
  - LR only (63%, 5/8)
  - LR + DM (75%, 9/12)
  - DM only (50%, 4/8)
- **By mucosal subsite:**
  - Oral cavity (54%, 7/13)
  - Oropharynx (75%, 6/8)
  - Hypopharynx (67%, 2/3)
  - Larynx (75%, 3/4)

Among HPV-neg pts (n=28 evaluable):

- Median PFS not reached
- 57% (16/28) of pts with PFS>6 months
- 56% (10/18) responses occurred at the 1st post-baseline scans after 6 weeks
- In 5 pts, time to response was >5 months

Safety

Figure 3: Incidence of treatment-related adverse events (AEs)



AEs of Interest:

- **Skin toxicity**
  - Acneiform rash in 76% (10% G3)
- **Mucosal bleeding**
  - Generally low-grade without need for dose interruptions
  - 1xG3 related tracheal hemorrhage

Treatment-related AEs leading to:

- Dose interruption: 16/42 (38%)
- Dose reduction: 4/42 (10%)
- Permanent discontinuation: 6/42 (14%)

Data from open database, as of 11-Dec-2023

CONCLUSIONS

- BCA101 + pembrolizumab has demonstrated a manageable safety profile.
- Overall response rate of 54% in the efficacy evaluable population, 64% in HPV-negative patients.
- mPFS for HPV-neg not reached, but 57% (16/28) of pts with PFS>6 months
- Among HPV-negative patients, responses were observed across all mucosal subsites and CPS subgroups (CPS 1-19 and ≥20), and in both distant metastatic and locoregionally advanced disease.
- Data warrants further evaluation of BCA101 in combination with anti-PD1 therapy in HPV-negative patients in a randomized study.

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BCA101 is an investigational therapy not approved for use in any country.

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