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Neoadjuvant APG-157 monotherapy in patients with locally advanced squamous cell carcinoma of head and neck: A phase IIA, Single Arm Trial

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BACKGROUND

Head and Neck Squamous Cell Carcinoma (HNSCC) carries significant morbidity and mortality. In 2024, over 71,000 new U.S. cases and 16,000 deaths are expected. Most patients present with **locally advanced HNSCC (LA-HNSCC),** where five-year survival rates remain approximately 40-50% in oral cavity and 30-40% (HPV-) or 60-70% (HPV+) oropharyngeal cancer despite aggressive treatment.

A 4–6-week treatment delay can cause tumor growth and upstaging due to HNSCC's rapid progression. Despite curative surgery and chemoradiotherapy, 25–50% of patients—especially HPV-negative—recur within a year. Current treatments are highly morbid, often leading to disfigurement, speech loss, and swallowing difficulties.

No FDA-approved neoadjuvant therapies exist for LA-HNSCC. An effective, safe neoadjuvant option in newly diagnosed patients could:

- Shrink or stabilize tumors to enable de-intensified surgery, radiation, or chemotherapy
- Preserve speech/swallowing and reduce treatment-related morbidity
- Lower recurrence risk and improve event-free & long-term survival

PHASE 2A STUDY (NCT05312710) DESIGN

Diagnosis of cancer — APG-157 Administration for 4 to 6 Weeks — **Definitive treatment**

Orally given 600 mgs (200 mgsX3 times) / day, supported by PK data

STUDY OBJECTIVES

Stop tumor growth and/or shrink tumor
Modulate tumor microenvironment to improve success of definitive treatment
Reduce post-treatment morbidity and increase survival

BASELINE CHARACTERISTICS (n=24)

Sex, n(%)	
Male	20 (83.3%)
Female	4 (16.7%)
Median (min, max) age,	65 (42, 89)

Race, n(%)	
White	15 (62.5%)
Hispanic	2 (8.3%)
African American	6 (25%)
African Indian	1 (4.2%)

Smoker, n (%)	
Current + Cannabis	11 (45.8%) + 2(8.3%)
Former +/- Cannabis	5 (20.8%)
Never	6 (25%)

Primary tumor site, n(%)	
Oral cavity	13 (54.2%)
Oropharynx	11 (45.3%)

P16 status	
Negative	9 (37.5%)
Positive	14 (58.3%)
Equivocal	1 (4.2%)

Clinical T staging	
T1	5 (20.8%)
T2	7 (29.2%)
T3	7 (29.2%)
T4	5 (20.8%)

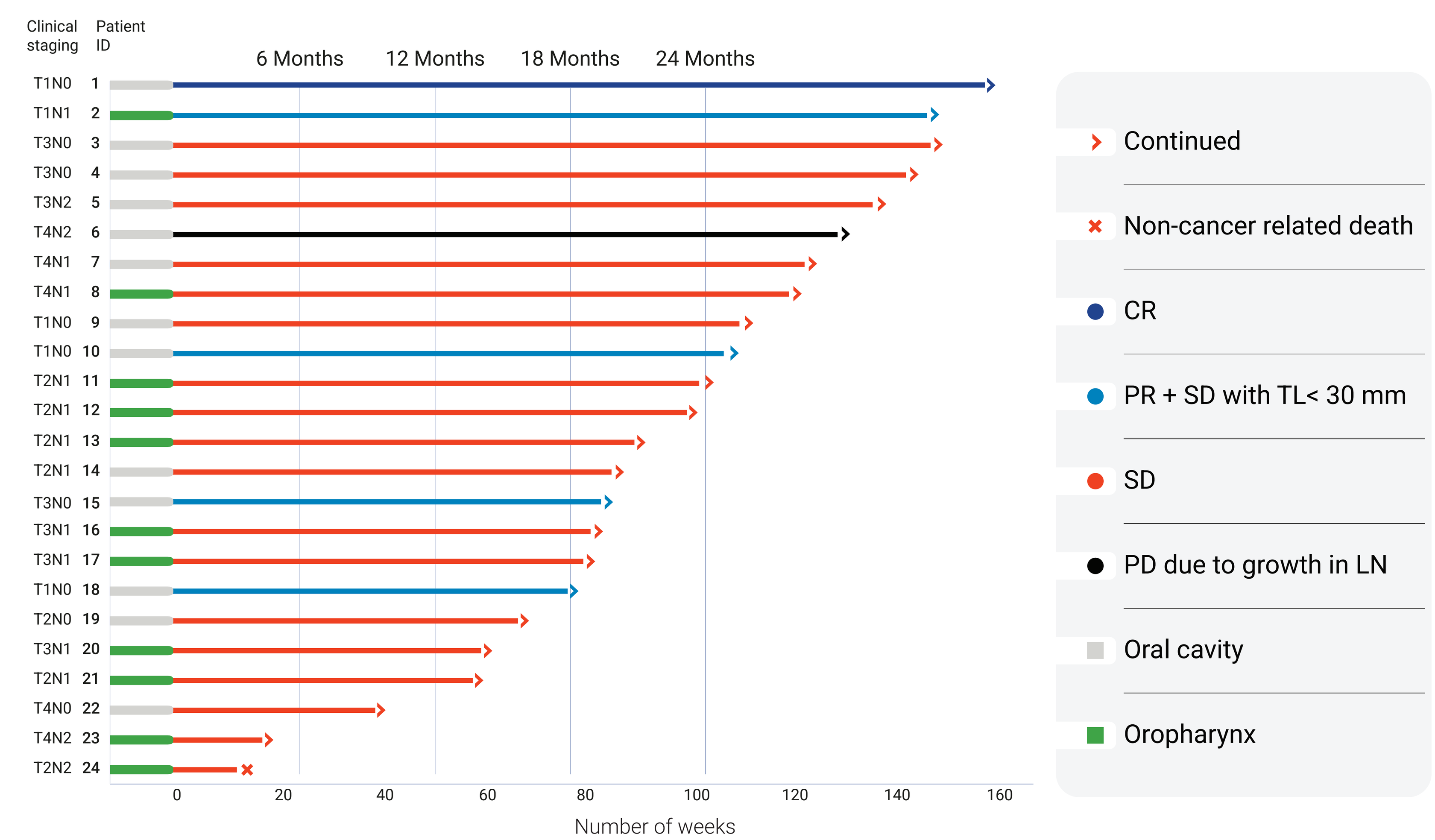
Clinical N staging	
N0	9 (37.5%)
N1	11 (45.8%)
N2	4 (16.7%)

Overall staging	
Stage I or II	11 (45.8%)
Stage III or IVA	13 (54.2%)

RESULTS

EVENT FREE SURVIVAL (EFS)

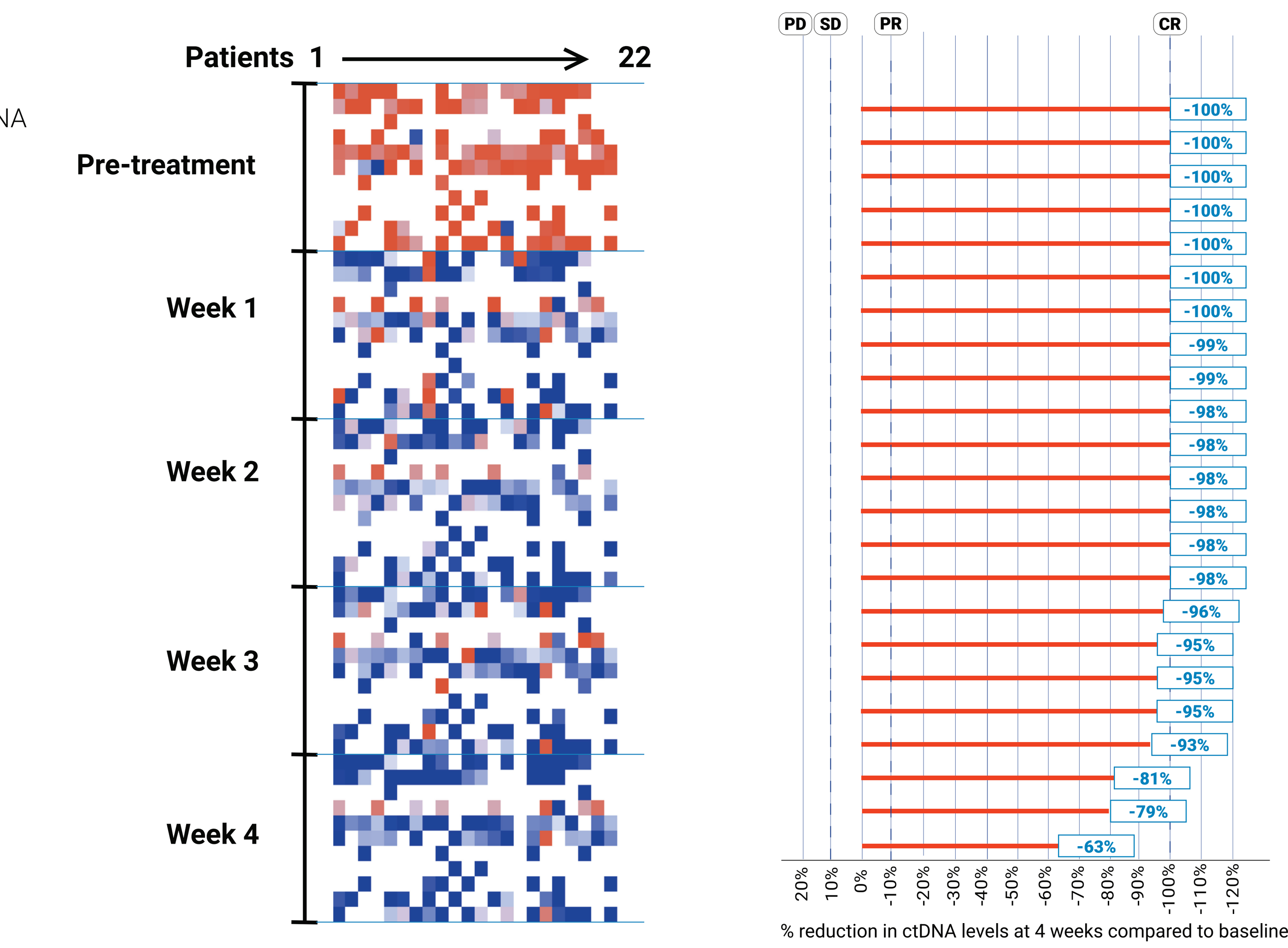
- 96% (23/24) alive & recurrence-free at median 90.1-week follow-up
- One death due to a non-cancer-related cause
- 11 recurrence-free ≥1 year, 10 ≥2 years



Clinical staging
Patient ID
6 Months
12 Months
18 Months
24 Months
T1N0 1
T1N1 2
T3N0 3
T3N0 4
T3N2 5
T4N2 6
T4N1 7
T4N1 8
T1N0 9
T1N0 10
T2N1 11
T2N1 12
T2N1 13
T2N1 14
T3N0 15
T3N1 16
T3N1 17
T1N0 18
T2N0 19
T3N1 20
T2N1 21
T4N0 22
T4N2 23
T2N2 24
0
20
40
60
80
100
120
140
160
Number of weeks
Continued
Non-cancer related death
CR
PR + SD with TL< 30 mm
SD
PD due to growth in LN
Oral cavity
Oropharynx

ctDNA CLEARANCE ON NEOADJUVANT APG-157

- 80% patients achieved >90% reduction in ctDNA



Patients 1 22
Pre-treatment
Week 1
Week 2
Week 3
Week 4
PD
SD
PR
CR
-100%
-100%
-100%
-100%
-100%
-100%
-100%
-99%
-99%
-98%
-98%
-98%
-98%
-98%
-98%
-96%
-95%
-95%
-95%
-93%
-81%
-79%
-63%
20%
10%
0%
-10%
-20%
-30%
-40%
-50%
-60%
-70%
-80%
-90%
-100%
-110%
-120%
% reduction in ctDNA levels at 4 weeks compared to baseline

RESPONSE ASSESSMENT USING RECIST V1.1

- Disease Control Rate (DCR): 95.8%
- Overall Response Rate (ORR): 16.7% with 2 Complete Response (CR) and 2 Partial Response (PR)
- Tumor regression: 45% showed reduction in the size of primary lesion



STABLE DISEASE
COMPLETE AND PARTIAL RESPONSE
% Change in Tumor Size at 4 weeks
30%
20%
10%
0%
-10%
-20%
-30%
-40%
-50%
-60%
-70%
-80%
-90%
-100%
-110%
20% PD
-30% PR
16.67%
11.90%
3.64%
2.38%
0.00%
0.00%
0.00%
0.00%
0.00%
0.00%
0.00%
0.00%
-2.27%
-3.81%
-4.35%
-4.50%
-11.20%
-13.64%
-22.22%
-27.27%
-31.25%
-33.30%
-100.0%
-100.0%
§
*

§Target lesion SD, time point response PD due to appearance of a new lymph node lesion; patient previously treated ovarian cancer
*Anti-tumor activity based on pathology as post-treatment radiographic scan was not available.

CLINICAL TO PATHOLOGICAL DOWNSTAGING (Surgical Subsets)

- 46.2% (6 of 13 patients with oral cavity) showed clinical to pathological downstaging

Patient IDs	Pre APG-157 Clinical Staging	Post APG-157 Pathological Staging
1	T1N0M0	pT1N0M0
3	T3N0M0	pT3N0M0
4	T3N0M0	pT3N0M0
5	T3N2M0	pT2N1M0
6	T4N2M0	pT4pN2M0
7	T4N1M0	pT1N0M0
9	T1N0M0	pT0(Tis)N0M0

Patient IDs	Pre APG-157 Clinical Staging	Post APG-157 Pathological Staging
10	T1N0M0	pT0(Tis)N0M0
14	T2N1M0	pT2N0M0
15	T3N0M0	pT1N0M0
18	T1N0M0	pT1N0M0
19	T2N0M0	pT4bN0M0
22	T4N0M0	pT4aN0M0

Downstaging | Stable | Upstaging

CONCLUSIONS

01 **Event-Free Survival -** 96% (23/24) remain alive and recurrence-free at median 90.1-week follow-up. 1 death due to a non-cancer-related cause. 10 of 20 patients who remained alive surpassed the 12-month survival mark had Stage III/V disease

02 **>80% patients achieved >90% ctDNA clearance prior to definitive therapy** as a surrogate to EFS

03 **No drug-related Grade ≥ 3** treatment emergent adverse events (TEAEs).

04 **No primary tumor progression** in any subject while on APG-157. **45% (11/24)** subjects experienced tumor reduction

05 **No delay in subsequent definitive therapy** with tumor-free resection margins

06 **46.2% (6/13)** of surgical patients had **clinical-to-pathological downstaging**

07 **Single agent activity.** Overall Response Rate (ORR) of 16.7% (4/24): CRs and 2 PRs. ORR is 23% in oral cavity, 33% p16 negative oral cavity cancer and 9.1% in oropharyngeal cancer

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"This poster contains non-enabling illustrative data for conceptual discussion only. Technical details are confidential and can be disclosed under mutual NDA/CDA."

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