PHASE 2, RANDOMIZED, DOUBLE-BLIND TRIAL OF EC-18 VERSUS PLACEBO TO MITIGATE THE DEVELOPMENT AND TIME COURSE OF ORAL MUCOSITIS FROM CONCOMITANT CHEMORADIATION FOR HEAD AND NECK CANCER

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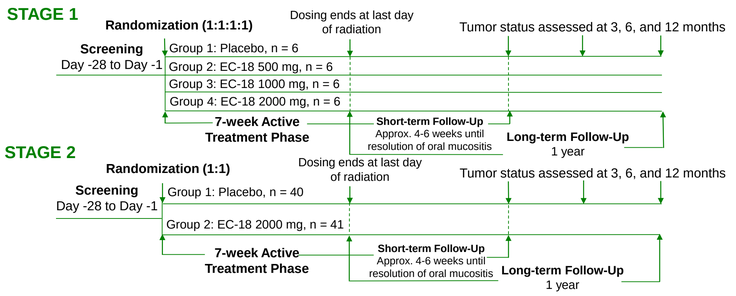
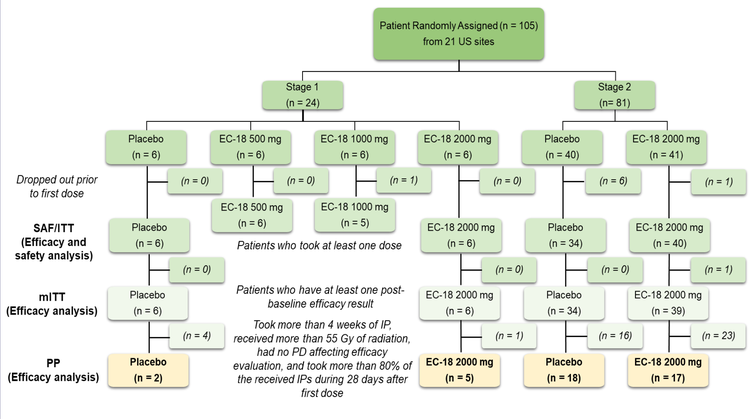
BACKGROUND AND METHODS

- Oral mucositis (OM) is one of the most common and debilitating side effects of Concomitant chemoradiotherapy (CRT), a standard of care for head and neck cancer (HNC) patients.
- Severe OM (SOM), defined as Grade 3 or 4 based on WHO, impacts ~70% of CRT patients.
- Currently, there are no approved drugs for OM in solid tumors.
- EC-18, an orally available, lipid-based small molecule with an immunomodulatory effect, may effectively mitigate SOM by minimizing the CRT-induced innate immune response.



- Patients (n = 105) with squamous cell cancers of the mouth, oropharynx, hypopharynx, or nasopharynx who received intensity-modulated radiation therapy (IMRT; with ≥ 55 Gy on ≥ 2 oral sites) and weekly or tri-weekly cisplatin were studied.
- WHO OM grade was assessed twice weekly during IMRT and then once weekly during the Short-term Follow-up (STFU) phase.
- SOM duration, incidence, and time to first opioid use were assessed for primary and secondary efficacy endpoints in the compliant per-protocol population (PP) for both Stages.
- PP population was analyzed to assess accurate efficacy during the COVID-19 pandemic, which negatively affected patient compliance and planned radiation.

PATIENT ANALYSIS SET



CONCLUSION

- EC-18 appeared to be **safe and well-tolerated** at twice-daily doses of 1000 mg (total daily dose of 2000 mg).
- Among patients in the PP population, **EC-18 appeared to effectively mitigate the duration, incidence, and time to onset of SOM**.
- The efficacy signal was especially notable among patients who were **HPV+ and received weekly cisplatin regimens**.

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SAFETY RESULTS

EC-18 demonstrated comparable safety across all arms

- A total of 12 serious adverse events (SAEs) in 8 (34.8%) subjects and 35 SAEs in 15 (20.3%) subjects were reported in Stage 1 and Stage 2, respectively.
- **None of the SAEs were determined to be attributable to EC-18**.
- Overall, AE in the 2000 mg PP arm (94.8%) was comparable to the 2000 mg ITT cohort (96.7%) and attributable to CRT.

Table 1: Treatment-Related AE ≥15%

	Placebo (N=40)	EC-18 500 mg (N=6)	EC-18 1000 mg (N=5)	EC-18 2000 mg (N=46)	Total (N=97)
	No. of patients (%)				%
Any Adverse Events	37 (92.5)	6 (100)	5 (100)	44 (95.7)	94.8
Nausea	28 (70.0)	4 (66.7)	2 (40)	32 (69.6)	68.0
Fatigue	17 (42.5)	3 (50.0)	0.0	20 (43.5)	41.2
Dry mouth	13 (32.5)	3 (50.0)	1 (20.0)	20 (43.5)	38.1
Dysgeusia	14 (35.0)	2 (33.3)	2 (40.0)	18 (39.1)	37.1
Dysphagia	16 (40.0)	2 (33.3)	1 (20.0)	16 (34.8)	36.1
Stomatitis	9 (19.6)	3 (50.0)	2 (40.0)	14 (30.4)	28.9
Vomiting	13 (28.3)	2 (33.3)	0.0	12 (26.1)	27.8
Constipation	12 (30.0)	3 (50.0)	0.0	10 (21.7)	25.8
Weight decreased	11 (23.9)	2 (33.3)	3 (60.0)	9 (19.6)	25.8
Oral pain	8 (20.0)	3 (50.0)	3 (60.0)	9 (19.6)	23.7
Oropharyngeal pain	9 (22.5)	4 (66.7)	0.0	8 (17.4)	21.6
Radiation skin injury	10 (21.7)	0.0	1 (20.0)	10 (21.7)	21.6
Diarrhoea	9 (22.5)	2 (33.3)	0.0	6 (13.0)	17.5
Dehydration	9 (22.5)	1 (16.7)	2 (40.0)	3 (6.5)	15.5

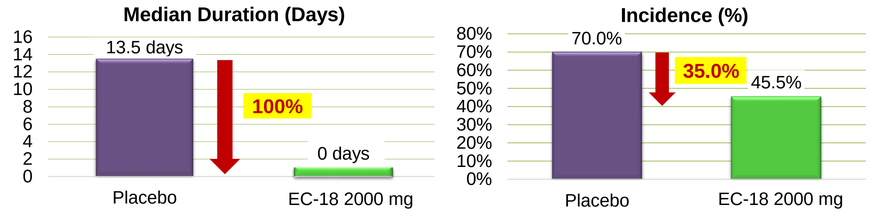
FUTURE PLAN

- One-year long-term follow-up or tumor assessment and biomarker analysis are ongoing.
- Genomics analysis is planned.

EFFICACY RESULTS

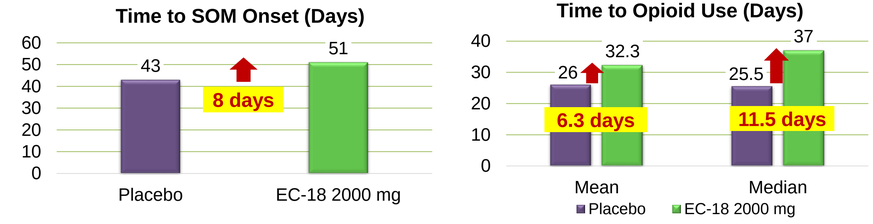
EC-18 reduced the median duration of SOM by 100% and the incidence of SOM by 35% compared to Placebo

Figure 1: Duration and Incidence of SOM through STFU Period - WHO Criteria (PP Population)



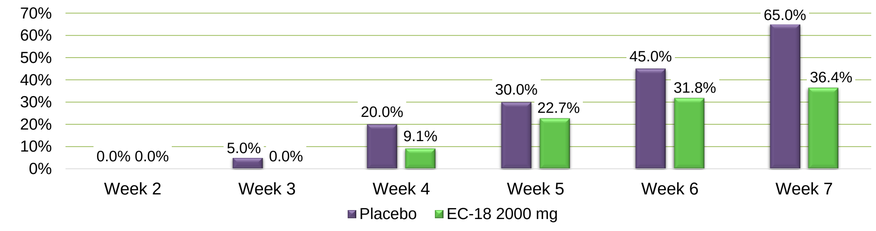
EC-18 reduced time to SOM onset by 8 days and time to opioid use by 6.3 days (mean) and 11.5 days (median)

Figure 2: Time to SOM onset and Opioid Use (PP Population)



Cumulative SOM Incidence of EC-18 treated patients was less than Placebo throughout the active treatment period

Figure 3: Cumulative incidence of SOM during Active Treatment Period (PP Population)



EC-18 favorably impacted SOM incidence in patients with HPV+ tumors and patients treated with weekly low-dose cisplatin regimen

Table 2: Incidence of SOM up to STFU for the Selected Subgroup of HNC Subjects (PP Population)

Subgroups (%)	EC-18 2000mg	Placebo	Chi-square Test p-value
HPV+	35.3% (6/17)*	66.7% (8/12)	0.09
HPV-	75.0% (3/4)	71.4% (5/7)*	0.90
Cisplatin (Weekly)	37.5% (6/16)	70.0% (7/10)	0.10
Tri-Weekly Cisplatin	66.7% (4/6)	70.0% (7/10)	0.90

* One unknown HPV Status