

Supplemental Table 1. Interval Adverse Event and Dosing Adjustment Schedule Based on CTCAE v4.0, for *N*-Acetylcysteine or Placebo

Adverse Event	Dose Adjustment
≥Grade 2 abdominal pain associated with gargling the agent	Discontinue gargling the agent. Route is changed to oral swish for 60 s followed by spitting the agent; if persists, change schedule to as needed for thickened secretions
≥Grade 2 gastric, esophageal, or lower gastrointestinal hemorrhage	Discontinue gargling the agent. Route is changed to oral swish for 60 s followed by spitting the agent; if persists, change schedule to as needed for thickened secretions
≥Grade 2 gastric, esophageal, or lower intestinal ulcer	Discontinue gargling the agent. Route is changed to oral swish for 60 s followed by spitting the agent; if persists, change schedule to as needed for thickened secretions
≥Grade 2 nausea immediately associated with gargling the agent	Discontinue gargling the agent. Route is changed to oral swish for 60 s followed by spitting the agent; if persists, change schedule as needed for thickened secretions
≥Grade 3 mucositis pain immediately associated with gargling or swishing the agent	Change the agent from scheduled 5 times/d to use as needed for thickened secretions
≥Grade 2 allergic reaction	Discontinue the agent

Abbreviation: CTCAE v4.0, Common Terminology Criteria for Adverse Events, version 4.0.

Supplemental Table 2. Linear Regression Model Results for Changes From Baseline for Both GRIX and QLQ H&N Surveys

Dependent Variable ^a	Change	No. of Patients	Study	Arm <i>P</i> Value ^b	Estimate
			Arm		From Lasso Regression ^c
GRIX xerostomia daytime	Baseline to end of RT	20		.55	—
	Baseline to 14 d post RT	15	−6.2	.32	—
GRIX xerostomia nighttime	Baseline to end of RT	21	12.4	.41	—
	Baseline to 14 d post RT	16	0.7	.98	—
GRIX xerostomia total score	Baseline to end of RT	20	−0.9	.93	−22.2
	Baseline to 14 d post RT	15	−12.7	.45	−41.6
GRIX sticky saliva daytime	Baseline to end of RT	21	−5.9	.62	—
	Baseline to 14 d post RT	16	−23.1	.14	−34.6
GRIX sticky saliva nighttime	Baseline to end of RT	21	−3.4	.81	—
	Baseline to 14 d post RT	16	−21.9	.22	−28.0
GRIX sticky saliva total score	Baseline to end of RT	21	−4.9	.68	—
	Baseline to 14 d post RT	16	−22.6	.16	−33.4
QLQ H&N pain	Baseline to end of RT	18	10.9	.52	—
	Baseline to 14 d post RT	10	12.3	.65	—

QLQ H&N swallowing	Baseline to end of RT	17	-16.2	.23	—
	Baseline to 14 d post RT	9	-1.4	.95	—
QLQ H&N teeth	Baseline to end of RT	18	0.7	.94	—
	Baseline to 14 d post RT	11	5.5	.62	—
QLQ H&N opening mouth	Baseline to end of RT	18	-11.0	.44	—
	Baseline to 14 d post RT	11	-30.6	.19	-96.9
QLQ H&N dry mouth	Baseline to end of RT	18	9.3	.63	—
	Baseline to 14 d post RT	11	2.2	.91	-83.8
QLQ H&N sticky saliva	Baseline to end of RT	18	-1.1	.94	—
	Baseline to 14 d post RT	10	-23.3	.17	-43.8
QLQ H&N senses problems	Baseline to end of RT	18	18.2	.01	4.9
	Baseline to 14 d post RT	11	22.1	.02	7.8
QLQ H&N coughing	Baseline to end of RT	18	7.2	.54	—
	Baseline to 14 d post RT	11	21.3	.33	—
QLQ H&N speech problems	Baseline to end of RT	17	-5.5	.64	-24.2
	Baseline to 14 d post RT	9	-9.4	.68	—
QLQ H&N felt ill	Baseline to end of RT	18	-16.7	.23	—
	Baseline to 14 d post RT	11	10.4	.64	—

QLQ H&N trouble with social contact	Baseline to end of RT	17	10.6	.16	—
	Baseline to 14 d post RT	8	2.6	.71	—
QLQ H&N trouble with social eating	Baseline to end of RT	17	-18.6	.12	—
	Baseline to 14 d post RT	7	10.8	.52	—
QLQ H&N less sexuality	Baseline to end of RT	16	-14.9	.20	—
	Baseline to 14 d post RT	8	-9.5	.65	—
QLQ H&N pain killers	Baseline to end of RT	17	21.1	.21	20.9
	Baseline to 14 d post RT	10	1.3	.95	—
QLQ H&N nutritional supplements	Baseline to end of RT	17	10.2	.67	—
	Baseline to 14 d post RT	10	43.3	.38	-11.9
QLQ H&N feeding tube	Baseline to end of RT	17	9.7	.64	—
	Baseline to 14 d post RT	10	16.7	.62	15.1
QLQ H&N weight loss	Baseline to end of RT	17	-29.2	.26	—
	Baseline to 14 d post RT	10	-14.0	.73	—
QLQ H&N weight gain	Baseline to end of RT	17	3.5	.84	—

Baseline to 14 d post RT	10	12.7	.68	-12.8
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Abbreviations: GRIX, Groningen Radiation-Induced Xerostomia; QLQ H&N, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Head and Neck; RT, radiotherapy.

^a To avoid overfitting, models are adjusted only for RT intent.

^b Bold indicates that the *P* value favors the NAC arm.

^c Lasso models include arm, age, sex, RT intent, primary tumor site, chemotherapy treatment, and mean dose of salivary total as possible covariates. Dashes indicate arm was not selected in the lasso regression model.

Supplemental Table 3. Repeated Measures Model Results for Both the GRIX and QLQ H&N Surveys

Dependent Variable^a	Arm Estimate	Arm P Value^b
GRIX xerostomia daytime	15.5	.05
GRIX xerostomia nighttime	8.0	.33
GRIX xerostomia total score	14.3	.06
GRIX sticky saliva daytime	20.1	.04
GRIX sticky saliva nighttime	12.5	0.14
GRIX sticky saliva total score	17.01	.05
QLQ H&N pain	5.3	0.41
QLQ H&N swallowing	14.3	.05
QLQ H&N teeth	-0.3	0.73
QLQ H&N opening mouth	11.4	0.07
QLQ H&N dry mouth	11.3	0.26
QLQ H&N sticky saliva	18.9	.02
QLQ H&N senses problems	-4.1	0.43
QLQ H&N coughing	-0.04	>.99
QLQ H&N speech problems	1.0	.90
QLQ H&N felt ill	6.6	.29
QLQ H&N trouble with social contact	-0.6	.89
QLQ H&N trouble with social eating	8.3	.25
QLQ H&N less sexuality	-2.1	.78
QLQ H&N pain killers	0.7	.94
QLQ H&N nutritional supplements	0.6	.96
QLQ H&N feeding tube	11.0	.39
QLQ H&N weight loss	19.7	.02

QLQ H&N weight gain

-1.9

.72

Abbreviations: GRIX, Groningen Radiation-Induced Xerostomia; QLQ H&N, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Head and Neck; RT, radiotherapy.

^a Models are adjusted for age, sex, RT intent, primary tumor site, chemotherapy treatment, and mean dose to salivary total.

^b Bold indicates that the *P* value favors the NAC arm.

Supplemental Figure. Scores of European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Head and Neck-35 Questions by Study Arm. A, Swallowing score (area under the curve for first 3 cycles, $P=.17$). B, Sticky saliva score ($P=.48$). C, Weight loss score ($P=.28$). For cycle numbers, 0 indicates baseline; 1-8 indicate weekly measurements during RT; 9-11 indicate 14, 45, 90 days post RT, respectively. In figure, A indicates placebo group; B, NAC group. NAC indicates *N*-acetylcysteine; RT, radiotherapy.

