

Supplemental Online Content

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eTable 1. Quality of life scores

eTable 2. Follow-up hematologic findings

eAppendix. Patients who did not receive protocol treatment

This supplemental material has been provided by the authors to give readers additional information about their work.

eTable 1. Quality of life scores and clinically meaningful decline at 1-year by instrument and domain.

Variable	RT Arm (n=30) Mean ± SD	TOS + ND Arm (n=31) Mean ± SD	P-value	RT Arm (n=30) % ¹	TOS + ND Arm (n=31) % ¹	P-value
MD Anderson Dysphagia Inventory (MDADI)						
Global	86.3 ± 18.9	87.5 ± 17.7	0.85	18.8	31.3	0.69
Emotional	84.9 ± 16.6	84.8 ± 14.9	0.98	6.3	18.8	0.60
Functional	87.3 ± 14.9	88.8 ± 13.3	0.77	13.3	25.0	0.65
Physical	85.0 ± 16.8	81.7 ± 17.9	0.59	20.0	43.8	0.25
Total	85.7 ± 15.6	84.7 ± 14.5	0.85	6.7	25.0	0.33
Composite (Excl. Global)	85.7 ± 15.6	84.5 ± 14.5	0.83	6.7	25.0	0.33
EORTC Core 30						
Global Health Status	79.4 ± 20.3	87.0 ± 17.2	0.24	31.3	12.5	0.39
Physical Functioning	6.3 ± 10.5	5.4 ± 12.5	0.82	25.0	12.5	0.65
Role Functioning	10.5 ± 15.9	6.3 ± 14.8	0.42	31.3	18.8	0.69
Emotional Functioning	13.6 ± 17.8	5.2 ± 8.0	0.077	6.3	6.3	> 0.99
Cognitive Functioning	6.1 ± 11.4	3.1 ± 6.7	0.34	12.5	12.5	> 0.99
Social Functioning	4.4 ± 15.6	4.2 ± 11.4	0.96	12.5	12.5	> 0.99
Fatigue	16.4 ± 21.1	12.5 ± 14.6	0.53	31.3	37.5	0.71
Nausea and Vomiting	0.0	1.0 ± 4.2	0.33	0.0	6.3	> 0.99
Pain	11.4 ± 13.7	9.4 ± 21.9	0.75	25.0	18.8	> 0.99
Dyspnea	1.8 ± 7.6	8.3 ± 14.9	0.13	6.3	6.7	> 0.99
Insomnia	10.5 ± 19.4	20.8 ± 24.0	0.18	18.8	31.3	0.69
Appetite Loss	3.5 ± 15.3	8.3 ± 14.9	0.35	6.3	25.0	0.33
Constipation	3.5 ± 10.5	8.3 ± 14.9	0.29	0.0	12.5	0.48
Diarrhea	0.0	0.0	--	0.0	0.0	--
Financial Difficulties	8.8 ± 21.8	10.4 ± 29.1	0.85	6.3	12.5	> 0.99
EORTC Head-and-Neck 35						
Pain	9.6 ± 12.5	13.5 ± 23.1	0.55	18.8	12.5	> 0.99
Swallowing	7.6 ± 9.2	7.3 ± 12.9	0.94	18.8	18.8	> 0.99
Senses	21.1 ± 21.4	12.5 ± 15.5	0.18	56.3	37.5	0.29
Speech	9.4 ± 13.0	7.6 ± 13.3	0.70	25.0	25.0	> 0.99
Social Eating	6.6 ± 12.0	9.9 ± 16.4	0.51	6.3	25.0	0.33
Social Contact	6.3 ± 11.2	2.1 ± 6.8	0.18	25.0	6.3	0.33
Less Sexuality	15.7 ± 22.5	7.1 ± 19.3	0.25	20.0	16.7	> 0.99
Teeth	5.3 ± 12.5	10.4 ± 20.1	0.38	6.3	18.8	0.60
Opening Mouth	7.0 ± 14.0	25.0 ± 33.3	0.058	25.0	31.3	> 0.99
Dry Mouth	38.6 ± 29.9	29.2 ± 20.6	0.28	43.8	43.8	> 0.99
Sticky Saliva	17.5 ± 23.2	22.9 ± 23.5	0.50	12.5	37.5	0.22
Coughing	10.5 ± 15.9	27.1 ± 21.8	0.018	6.3	37.5	0.083
Felt Ill	3.5 ± 10.5	4.2 ± 11.4	0.86	0.0	13.3	0.23
Pain Killers	15.8 ± 37.5	25.0 ± 44.7	0.52	12.5	12.5	> 0.99
Nutritional Suppl.	26.3 ± 45.2	37.5 ± 50.0	0.50	18.8	25.0	> 0.99
Feeding Tube	0.0	0.0	--	0.0	0.0	--
Weight Loss	0.0	25.0 ± 44.7	0.041	0.0	12.5	0.48
Weight Gain	47.4 ± 51.3	37.5 ± 50.0	0.57	37.5	31.3	0.71
Voice Handicap Index (VHI-10)						
Total	2.9 ± 5.2	3.7 ± 5.7	0.69	0.0	6.3	0.49
Neck Dissection Impairment Index (NDII)						
Total	88.3 ± 15.4	94.5 ± 8.5	0.14	7.1	26.7	0.33
EuroQoL 5-Dimension 5-Level (EQ-5D-5L)						
Health State	82.4 ± 14.7	86.9 ± 14.3	0.37	31.3	12.5	0.39
Index	0.91 ± 0.06	0.91 ± 0.08	0.83	0.0	6.3	> 0.99
Patient Neurotoxicity Questionnaire (PNQ)						
Numbness	0.8 ± 1.1	0.4 ± 0.7	0.37	14.3	0.0	0.50

Weakness	0.1 ± 0.4	0.3 ± 0.7	0.47	0.0	0.0	--
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RT – Radiotherapy; **TOS + ND** – Trans-oral surgery and neck dissection; **EORTC** – European Organization for Research and Treatment of Cancer; ¹Defined as decrease of at least 10 points (EORTC Core 30 Global Health Status and MDADI), decrease of at least 0.1 points (EQ-5D-5L Index) or increase of at least 10 points for all other items compared to baseline (PNQ reported as “severe” proportion)

eTable 2. Follow-up hematologic findings.

Characteristic	All Patients (n=61)	RT Arm (n=30)	TOS + ND Arm (n=31)	P- value
White blood cells – median (IQR)	5.50 (4.20, 6.30)	5.00 (3.70, 6.30)	5.65 (4.40, 6.40)	0.71
Neutrophils – median (IQR)	3.30 (2.30, 4.50)	3.00 (2.30, 4.50)	3.60 (2.55, 4.50)	0.75
Platelets – median (IQR)	195.0 (160.0, 220.0)	174.0 (159.0, 199.0)	204.5 (190.5, 227.5)	0.28
Hemoglobin – median (IQR)	139.0 (126.0, 152.0)	139.0 (131.0, 144.0)	144.0 (124.0, 155.0)	0.70
Blood urea nitrogen – median (IQR)	5.15 (3.90, 6.10)	4.00 (3.30, 6.30)	5.60 (4.90, 5.90)	0.26
Creatinine – median (IQR)	87.0 (72.0, 95.0)	91.0 (86.0, 96.0)	74.0 (66.0, 89.0)	0.042

RT – Radiotherapy; **TOS + ND** – Trans-oral surgery and neck dissection; **IQR** – Interquartile range

eAppendix.

Patients Who Did Not Receive Protocol Treatment

In the RT arm, this occurred for 1 patient, due to study closure between randomization and initiation of treatment. This patient received standard of care treatment and withdrew from the study. In the TOS+ND arm, this occurred for 4 patients. Of those four, two withdrew study consent prior to treatment, a third was brought to the operating room (OR) and the tumor was found to be inaccessible to TORS; and the fourth was not treated with surgery due to unavailability of OR access shortly after the start of the COVID-19 pandemic. Both of these latter two patients, after discussion with their physicians, opted to receive de-escalated RT. As part of the intention-to-treat analysis, all patients are analyzed in the arm to which they are randomized, but none had any survival or recurrence events. In addition, pandemic-related delays did not appear to negatively affect outcomes, as none of the patients enrolled between Mar-Jun 2020 had recurrence or death events.