AUCTORES
Globalize your Research

International Journal of Clinical Case Reports and Reviews
Shivani Malik *

Open Access

Research Article

# Optimizing Palliative Radiotherapy in Incurable Locally Advanced Head and Neck Squamous Cell Cancer [LAHNSCC]: A Prospective Comparison of Quad Shot and a Short Course Hypofractionated Regimen

**Shivani Malik *, Ashok Kumar Arya**

Senior resident, Department of Radiation Oncology, Sarojini Naidu Medical College, Agra, Uttar Pradesh, India.

***Corresponding Author:** Shivani Malik, Senior resident, Department of Radiation Oncology, Sarojini Naidu Medical College, Agra, Uttar Pradesh, India.

**Received Date:** July 07, 2026 | **Accepted Date:** July 21, 2026 | **Published Date:** August 07, 2026

**Citation:** Shivani Malik, Ashok K. Arya, (2026), Optimizing Palliative Radiotherapy in Incurable Locally Advanced Head and Neck Squamous Cell Cancer [LAHNSCC]: A Prospective Comparison of Quad Shot and a Short Course Hypofractionated Regimen, *International Journal of Clinical Case Reports and Reviews*, 36(5); **DOI:10.31579/2690-4861/1144**



## Abstract:

**Background:** Patients with incurable LAHNSCC often require palliative radiotherapy for symptom relief and quality-of-life [QOL]improvement; however, no standard hypofractionated regimen has been universally accepted.

**Objectives:** The primary objective of the study was to compare clinical response and QOL outcomes between the Quad Shot regimen [ARM A] and a short-course hypofractionated radiotherapy schedule [ARM B] in patients with incurable LAHNSCC following treatment completion and first follow-up assessment. Secondary objectives included comparison of treatment compliance, acute radiation toxicities, performance status improvement, supportive care requirements including Ryle's tube insertion, feasibility of subsequent palliative systemic therapy, and overall survival between the two treatment arms.

**Materials and Methods:** This prospective randomized comparative study included 70 patients with histologically confirmed incurable LAHNSCC randomized equally into two arms. Arm A received the (14.8 Gy/4 fractions over 2 days, repeated every 3 weeks for three cycles; total 44.4 Gy). Arm B received 20 Gy/5 fractions over 1 week, repeated after 3 weeks (total 40 Gy).

**Results:** Treatment completion was higher in Arm A than Arm B (80.0% vs. 71.4%). Partial response was observed in 96.4% and 96.0% of patients, respectively. Both regimens significantly improved Karnofsky Performance Status and quality-of-life scores ($p<0.001$). Grade 3 mucositis occurred in one patient in Arm A. Median overall survival was 4.0 months in Arm A and 3.5 months in Arm B.

**Conclusion:** Both regimens achieved effective palliation with acceptable toxicity. The Quad Shot regimen demonstrated better compliance and modest survival benefit, supporting its role in palliative management of incurable LAHNSCC.

**Keywords:** head and neck cancer; palliative radiotherapy; hypofractionation; quad shot; quality of life

## Introduction

Head and neck cancers remain among the most common malignancies worldwide and contribute substantially to cancer-related mortality, particularly in low- and middle-income countries. India carries a disproportionately high disease burden because of widespread tobacco consumption, delayed diagnosis, limited healthcare accessibility, and poor socioeconomic conditions. Squamous cell carcinoma constitutes the predominant histological subtype and frequently presents at an advanced stage with extensive locoregional disease.

Despite progress in surgical techniques, radiotherapy delivery, and systemic therapies, a significant proportion of patients with locally advanced head and neck squamous cell carcinoma (LAHNSCC) are not suitable candidates for curative treatment. Advanced age, poor performance status, severe malnutrition, unresectable disease, medical

comorbidities, and financial limitations commonly restrict aggressive multimodality management in this population.

For such patients, treatment intent is primarily palliative, focusing on alleviation of distressing symptoms, maintenance of oral intake and speech, preservation of functional independence, and improvement in overall quality of life. Patients with advanced head and neck malignancies frequently experience severe pain, dysphagia, bleeding, fetor, airway compromise, weight loss, and psychosocial impairment, all of which significantly affect daily functioning.

Palliative radiotherapy therefore represents an important component of supportive oncologic care in advanced incurable disease. Hypofractionated schedules are particularly attractive in this setting because they shorten overall treatment duration, reduce repeated hospital visits, improve treatment feasibility in frail individuals, and optimize utilization of limited radiotherapy resources.

Several hypofractionated regimens have demonstrated meaningful symptomatic benefit with acceptable toxicity profiles. Among these, the Quad Shot regimen and short-course schedules such as 20 Gy in 5 fractions are widely practiced in routine clinical settings. Earlier prospective investigations established the feasibility of these approaches, while more recent studies have continued to demonstrate favorable symptom control, quality-of-life improvement, and manageable treatment-related toxicities.

Validated assessment tools including the University of Washington Quality of Life Questionnaire version 4 and Radiation Therapy Oncology Group toxicity criteria are commonly employed to evaluate patient-reported outcomes and acute adverse effects in head and neck cancer patients receiving palliative radiotherapy.

However, an optimal hypofractionated palliative radiotherapy schedule for incurable LAHNSCC has not yet been universally established. Prospective comparative evidence remains limited, particularly from resource-constrained settings and Indian oncology centers. Therefore, the present prospective randomized study was conducted to compare clinical outcomes, treatment tolerability, quality-of-life improvement, and survival between the Quad Shot regimen and a short-course hypofractionated radiotherapy schedule in patients with incurable LAHNSCC.

## Materials and Methods

### General Study Details

This prospective randomized comparative study was conducted in the Department of Radiation Oncology at a tertiary care teaching institute in India between February 2024 and December 2025. The study was designed as an open-label parallel-arm trial comparing two hypofractionated palliative radiotherapy schedules in patients with incurable locally advanced head and neck squamous cell carcinoma (LAHNSCC).

The study protocol was approved by the Institutional Ethics Committee (IEC approval number: SNMC/IEC/2024/195; dated 2 February 2024). Written informed consent was obtained from all participants before enrolment. The study adhered to the ethical principles of the Declaration of Helsinki, Good Clinical Practice guidelines, and Indian Council of Medical Research ethical recommendations.

## Aims/Objectives

The primary objective of the study was to compare clinical response and quality-of-life outcomes between the Quad Shot regimen and a short-course hypofractionated radiotherapy schedule in patients with incurable LAHNSCC following treatment completion and first follow-up assessment.

Secondary objectives included comparison of treatment compliance, acute radiation toxicities, performance status improvement, supportive care requirements including Ryle's tube insertion, feasibility of subsequent palliative systemic therapy, and overall survival between the two treatment arms.

### Study Methodology

A total of 70 treatment-naïve patients with histopathologically confirmed LAHNSCC were enrolled during the study period. Patients attending the Radiation Oncology outpatient department who fulfilled the eligibility criteria were consecutively screened for inclusion.

Patients aged ≥18 years with unresectable stage IVA or IVB squamous cell carcinoma of the head and neck region who were unsuitable for curative treatment were eligible for enrolment. Additional inclusion criteria included Karnofsky Performance Status (KPS) >40, adequate hematological and biochemical parameters, and ability to provide informed consent.

Patients with distant metastases, prior surgery, chemotherapy or radiotherapy for head and neck malignancy, non-squamous histology, synchronous malignancy, uncontrolled comorbid illness, pregnancy, or inability to comply with treatment or follow-up were excluded.

Baseline demographic details, addiction history, tumor site, disease stage, nutritional status, and performance status were documented before treatment initiation.

### Randomization and Allocation

Eligible patients were randomized in a 1:1 ratio into two treatment groups using computer-generated random numbers. Allocation concealment was ensured using sequentially numbered opaque sealed envelopes prepared before study initiation, which were opened only after patient enrolment.

Blinding was not feasible because of the nature of the intervention. However, predefined response criteria, standardized toxicity grading systems, uniform treatment protocols, and scheduled follow-up assessments were used to reduce observer-related bias.

## Interventions

### Arm A: Quad Shot Regimen

Patients allocated to Arm A received hypofractionated radiotherapy to a total dose of 14.8 Gy delivered in 4 fractions of 3.7 Gy over 2 consecutive days, with two fractions administered daily at a minimum interval of 6 hours. The cycle was repeated every 3 weeks for a maximum of three cycles in the absence of disease progression or unacceptable toxicity, resulting in a planned cumulative dose of 44.4 Gy in 12 fractions.

### Arm B: Short-Course Hypofractionated Regimen

Patients in Arm B received external beam radiotherapy to a dose of 20 Gy in 5 daily fractions of 4 Gy over one week. Following a treatment interval

of 3 weeks, an identical second course was administered, resulting in a total planned dose of 40 Gy in 10 fractions.

### Radiotherapy Technique

All patients underwent conventional radiotherapy simulation in the supine position using appropriate immobilization devices. Treatment portals were planned to include the gross primary lesion and clinically or radiologically involved nodal regions with adequate margins. Parallel opposed lateral fields were predominantly employed.

Radiotherapy was delivered using Cobalt-60 teletherapy units, with dose prescription performed at the midplane along the central axis. Field reduction, shrinking portals, and spinal cord shielding were incorporated during subsequent phases of treatment whenever clinically indicated to maintain spinal cord dose within tolerance limits.

Supportive care measures including nutritional support, analgesics, oral hygiene measures, antibiotics, anti-inflammatory medications, and Ryle's tube insertion were provided according to individual patient requirements during treatment and follow-up.

### Baseline Evaluation

Pretreatment evaluation included detailed clinical history, physical examination, comprehensive head and neck assessment, and documentation of addiction history and associated comorbidities. Performance status was evaluated using the Karnofsky Performance Scale.

Baseline investigations included complete blood counts, renal and liver function tests, chest radiography, ultrasonography of the abdomen, and contrast-enhanced computed tomography of the head and neck region for locoregional staging.

Tumor staging was performed according to the American Joint Committee on Cancer (AJCC) 8th edition staging system.

### Response Assessment and Definitions

Clinical response assessment was performed using World Health Organization response criteria based on physical examination findings and symptomatic improvement at treatment completion and follow-up visits.

Complete response was defined as disappearance of all clinically detectable disease. Partial response was defined as ≥50% reduction in measurable disease burden. Stable disease was defined as <50% reduction or <25% increase in disease extent, whereas progressive disease was defined as ≥25% increase in tumor burden or development of new lesions.

Acute radiation-related toxicities were graded according to Radiation Therapy Oncology Group acute radiation morbidity criteria.

Treatment compliance was defined as completion of the planned radiotherapy schedule without permanent discontinuation. Overall survival was calculated from the date of randomization to the date of death or last follow-up.

Quality of life was assessed using the University of Washington Quality of Life Questionnaire version 4 (UWQOL v4), which evaluates multiple functional and psychosocial domains relevant to head and neck cancer patients. Performance status was assessed using the Karnofsky Performance Scale.

Assessments were performed at baseline, upon completion of radiotherapy, and at the first post-treatment follow-up visit approximately one month after treatment completion.

### Follow-up

Following completion of radiotherapy, patients were regularly evaluated in the outpatient department. Follow-up assessments included evaluation of symptom relief, treatment response, toxicities, nutritional status, supportive care requirements, and suitability for further palliative systemic therapy.

Radiological investigations during follow-up were performed selectively whenever clinically indicated rather than routinely, considering the palliative intent of treatment, patient compliance, and resource limitations.

### Statistics

Sample size estimation was based on anticipated differences in quality-of-life outcomes between the two treatment groups derived from previously published studies evaluating hypofractionated palliative radiotherapy schedules in head and neck cancers. Assuming a significance level (α) of 0.05 and statistical power of 80%, with adjustment for expected attrition in this palliative population, a minimum sample size of 28 patients per arm was calculated.

To account for possible treatment default, mortality, and loss to follow-up, the final sample size was increased to 35 patients per arm, resulting in a total study population of 70 patients.

Data were entered into Microsoft Excel and analyzed using Statistical Package for the Social Sciences (SPSS) software version 26.0 (IBM Corp., Armonk, NY, USA).

Continuous variables were expressed as mean ± standard deviation or median with range, while categorical variables were summarized as frequencies and percentages. Intergroup comparisons for categorical variables were performed using Chi-square test or Fisher's exact test, as appropriate. Paired comparisons within treatment groups were analyzed using paired Student's t-test. Survival analysis was performed using the Kaplan-Meier method, and differences between survival curves were assessed using the log-rank test.

A p-value <0.05 was considered statistically significant. Missing data resulting from treatment default or loss to follow-up were excluded from final response assessment wherever applicable.

## Results

### Patient Recruitment and CONSORT Flow

Between January 2024 and December 2025, a total of 86 patients with locally advanced head and neck squamous cell carcinoma were screened for eligibility. Of these, 70 patients fulfilling the inclusion criteria were enrolled and randomized equally into two treatment arms (35 patients in each arm). Eight patients did not meet inclusion criteria, while another eight declined participation or were unsuitable for enrolment due to poor general condition.

In Arm A (Quad Shot regimen), 28 patients (80.0%) completed the planned treatment schedule, whereas 7 patients (20.0%) defaulted during treatment or follow-up. In Arm B (short-course hypofractionated regimen), 25 patients (71.4%) completed treatment and 10 patients

(28.6%) defaulted. Patients who defaulted were excluded from final response assessment wherever complete follow-up data were unavailable.

The patient selection and treatment allocation process is summarized in the CONSORT flow diagram (Figure 1).

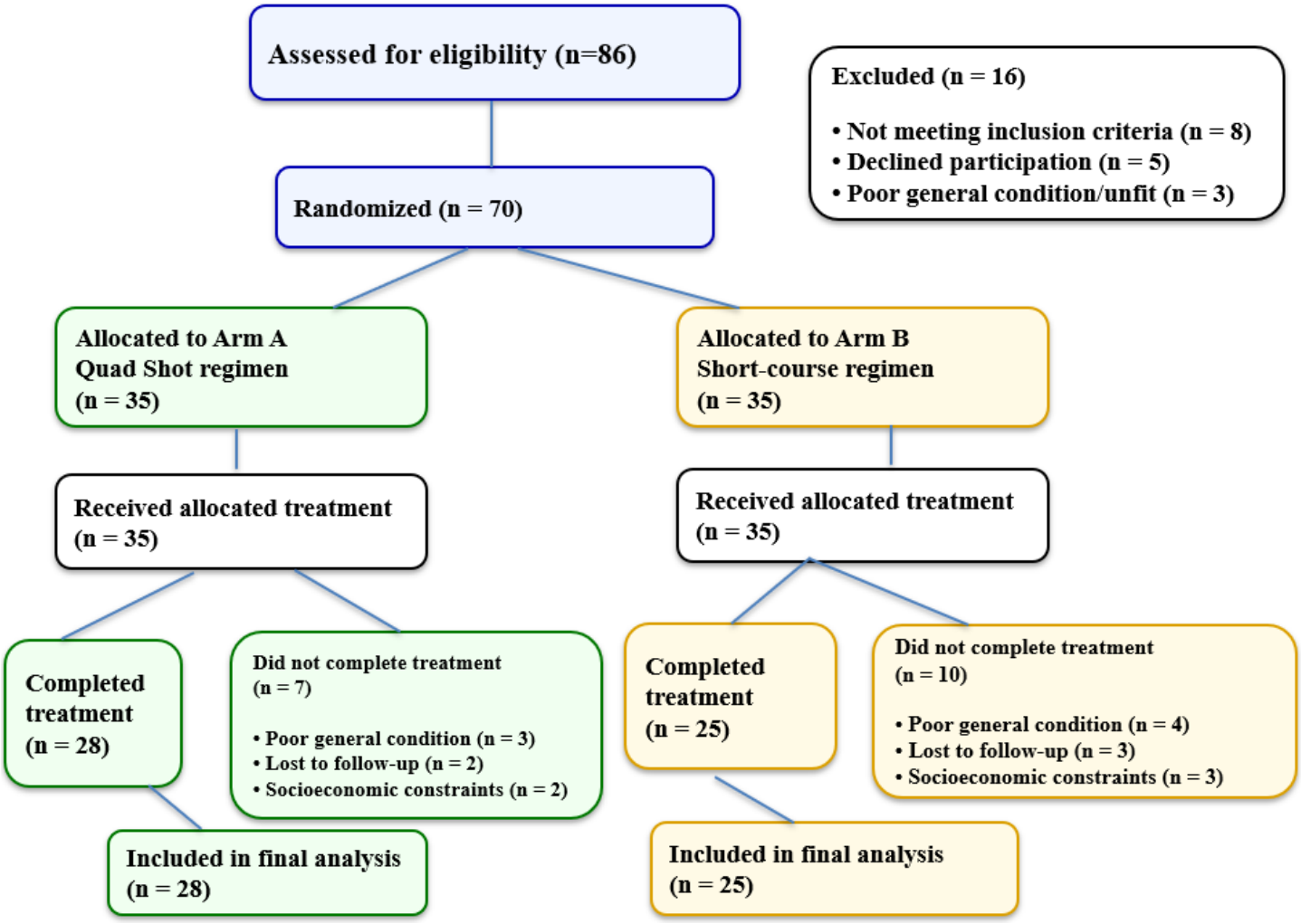


**Figure 1:** CONSORT Flow Diagram of Patient Recruitment, Treatment Allocation, and Analysis.

### Baseline Patient and Disease Characteristics

Baseline demographic and disease-related characteristics were comparable between the two treatment arms. The median age was 52.0 years in Arm A and 53.0 years in Arm B. Male predominance was observed in both groups. Tobacco use was the most common addiction history.

The oral cavity represented the predominant primary tumor site in both arms. Most patients presented with stage IVA or IVB disease and had poor baseline nutritional and performance status.These characteristics has been described in Table 1.

| Variable | Arm A (n=35) | Arm B (n=35) | p-value |
|---|---|---|---|
| Median age (years) | 52.0 | 53.0 | 0.684 |
| Male gender, n (%) | 30 (85.7) | 25 (71.4) | 0.142 |
| Tobacco use, n (%) | 30 (85.7) | 28 (80.0) | 0.518 |
| Smoking history, n (%) | 20 (57.1) | 24 (68.6) | 0.319 |
| Alcohol use, n (%) | 7 (20.0) | 2 (5.7) | 0.072 |
| Oral cavity primary, n (%) | 30 (85.7) | 27 (77.1) | 0.347 |
| Stage IVA disease, n (%) | 25 (71.4) | 17 (48.6) | 0.051 |
| Stage IVB disease, n (%) | 10 (28.6) | 18 (51.4) | 0.051 |

**Table 1:** Baseline patient and disease characteristics

### Treatment Compliance

Treatment completion was higher in the Quad Shot arm compared with the short-course hypofractionated arm (80.0% vs. 71.4%). Treatment default occurred in 7 patients in Arm A and 10 patients in Arm B.

The common causes of treatment non-compliance included poor performance status, progressive clinical deterioration, socioeconomic limitations, travel-related difficulties, and lack of caregiver support.

### Supportive Interventions

Nutritional compromise and dysphagia were common at presentation. Overall, 28 patients (40.0%) required Ryle's tube insertion either before or during treatment.

Requirement for enteral nutritional support was more frequently observed in patients with oral cavity and oropharyngeal malignancies associated with severe dysphagia and poor oral intake.

### Post-radiotherapy Palliative Chemotherapy

Improvement in performance status following radiotherapy enabled several patients to receive additional systemic therapy.

In Arm A, 12 patients (34.3%) received palliative chemotherapy following completion of radiotherapy, whereas 14 patients (40.0%) in Arm B subsequently received systemic treatment. The most commonly administered regimen was weekly methotrexate with or without oral gefitinib. A limited number of patients in Arm A additionally received paclitaxel-carboplatin–based chemotherapy.

Overall, 26 patients (49%) were able to tolerate further palliative systemic treatment after radiotherapy.

### Acute Toxicity Profile

Both treatment schedules were generally well tolerated. Most toxicities were Grade 1–2 mucositis and dermatitis managed conservatively with supportive care.

Grade 3 mucositis was observed in one patient (2.9%) in Arm A, while no patient in Arm B developed Grade 3 mucositis. No Grade 3 or higher dermatitis was observed in either arm. No treatment-related mortality occurred during the study period. All toxicities has been analysed in Table 2.

| Toxicity | Arm A (n=35) | Arm B (n=35) | p-value |
|---|---|---|---|
| Grade 1–2 mucositis, n (%) | 24 (68.6) | 23 (65.7) | 0.796 |
| Grade 3 mucositis, n (%) | 1 (2.9) | 0 | 0.314 |
| Grade 1–2 dermatitis, n (%) | 18 (51.4) | 20 (57.1) | 0.632 |
| Grade ≥3 dermatitis, n (%) | 0 | 0 | — |

**Table 2:** Acute radiation toxicity profile

### Clinical Tumor and Nodal Response

Clinical response assessment at treatment completion demonstrated high response rates in both treatment groups.

Partial response was observed in 27 of 28 evaluable patients (96.4%) in Arm A and 24 of 25 evaluable patients (96.0%) in Arm B. Stable disease was observed in one patient in each treatment arm. No patient demonstrated progressive disease during initial post-treatment assessment.

Complete nodal response was achieved in 75.0% of patients in Arm A and 72.0% in Arm B. Overall Response has been grouped in Table 3. Tumor response has been depicted in figure 2 and nodal response in figure 3.

| Response | Arm A (%) | Arm B (%) | p-value |
|---|---|---|---|
| Partial response | 96.4 | 96.0 | 0.948 |
| Stable disease | 3.6 | 4.0 | 0.948 |
| Progressive disease | 0 | 0 | — |
| Complete nodal response | 75.0 | 72.0 | 0.781 |

**Table 3:** Clinical response assessment

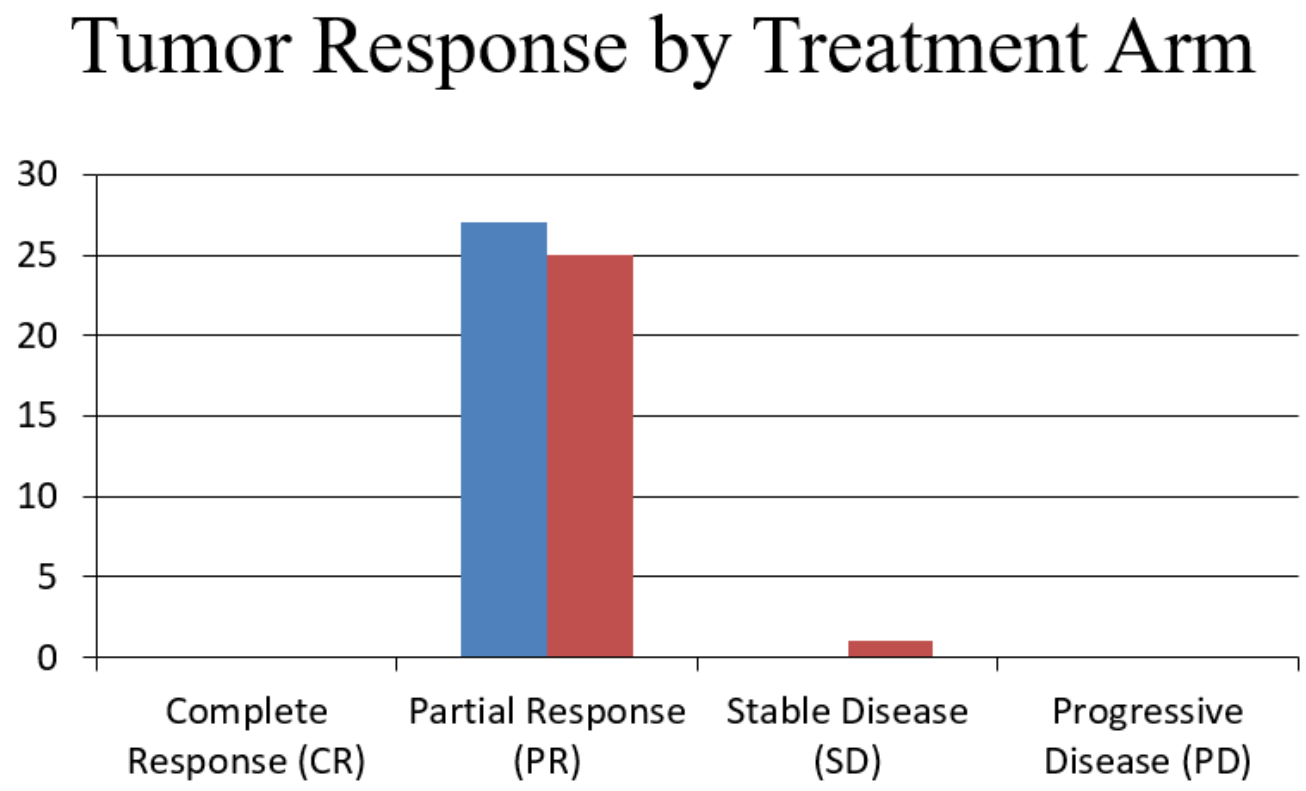


**Figure 2:** Overall Tumor response assessment.

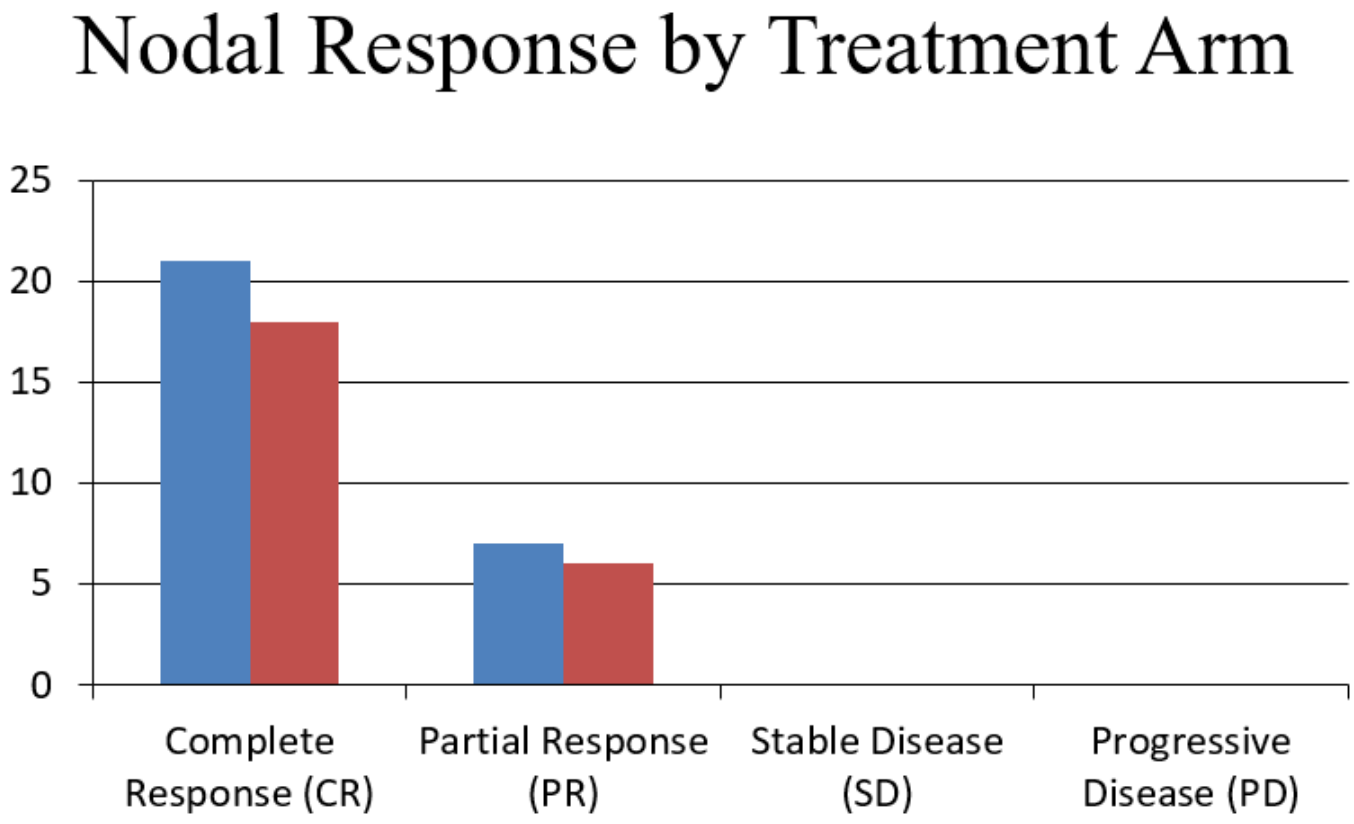


**Figure 3:** Overall Nodal response assessment.

### Performance Status Outcomes

A statistically significant improvement in Karnofsky Performance Status (KPS) was observed following treatment in both groups ($p<0.001$).

In Arm A, mean KPS improved from 47.9 ± 9.2 at baseline to 63.9 ± 7.9 post-treatment. In Arm B, mean KPS improved from 50.8 ± 11.5 to 64.0 ± 9.6 following treatment.

The magnitude of performance status improvement was marginally greater in the Quad Shot arm and this has been shown in Table 4.

| Parameter | Arm A | Arm B | p-value |
|---|---|---|---|
| Pretreatment KPS (mean ± SD) | 47.9 ± 9.2 | 50.8 ± 11.5 | 0.246 |
| Post-treatment KPS (mean ± SD) | 63.9 ± 7.9 | 64.0 ± 9.6 | 0.964 |
| Within-group improvement | p<0.001 | p<0.001 | — |

**Table 4:** Karnofsky Performance Status improvement

### Quality-of-Life Outcomes

Quality-of-life assessment using UWQOL version 4 demonstrated significant improvement across multiple functional and psychosocial domains following treatment in both arms.

Substantial improvement was observed in pain, swallowing, speech, activity, mood, anxiety, and social functioning scores. However, worsening of taste and salivary function was noted after radiotherapy in both treatment groups.

Overall quality-of-life scores improved from 22.5 ± 11.6 to 68.8 ± 19.9 in Arm A and from 22.6 ± 13.0 to 68.6 ± 18.6 in Arm B ($p<0.001$ for both groups). Greater improvement in pain relief and appearance-related scores was observed in patients treated with the Quad Shot regimen.Detailed domain-wise UWQOL analysis has been provided in Table 5.

| Domain | Arm A Pre (Mean ± SD) | Arm A Post | p-value | Arm B Pre | Arm B Post | p-value |
|---|---|---|---|---|---|---|
| Pain | 17.6 ± 11.6 | 88.6 ± 21.2 | <0.001 | 34.4 ± 14.4 | 89.7 ± 17.6 | <0.001 |
| Appearance | 38.2 ± 19.7 | 83.9 ± 15.3 | <0.001 | 37.5 ± 14.7 | 77.1 ± 12.6 | <0.001 |
| Activity | 38.4 ± 15.9 | 76.8 ± 16.6 | <0.001 | 42.7 ± 15.6 | 66.7 ± 17.6 | <0.001 |
| Recreation | 36.6 ± 15.9 | 68.8 ± 27.7 | <0.001 | 49.0 ± 11.6 | 69.8 ± 12.7 | <0.001 |
| Swallowing | 34.4 ± 19.3 | 66.8 ± 20.4 | <0.001 | 38.7 ± 16.3 | 72.5 ± 16.0 | <0.001 |
| Chewing | 16.1 ± 17.0 | 49.1 ± 35.0 | <0.001 | 19.8 ± 12.7 | 37.5 ± 22.1 | <0.001 |
| Speech | 34.5 ± 26.6 | 74.0 ± 24.6 | <0.001 | 33.0 ± — | 61.3 ± 12.9 | <0.001 |
| Shoulder | 3.0 ± 8.8 | 7.4 ± 15.4 | 0.096 | 1.3 ± 6.6 | 6.6 ± 13.5 | 0.043 |
| Taste | 45.1 ± 20.9 | 10.7 ± 22.4 | <0.001 | 41.5 ± 18.0 | 8.3 ± 14.6 | <0.001 |
| Saliva | 19.0 ± 24.8 | 4.7 ± 11.8 | <0.001 | 35.7 ± 9.4 | 2.6 ± 9.1 | <0.001 |
| Mood | 42.9 ± 19.1 | 77.7 ± 20.8 | <0.001 | 33.3 ± 19.0 | 67.7 ± 18.8 | <0.001 |
| Anxiety | 35.5 ± 18.1 | 72.7 ± 25.8 | <0.001 | 37.3 ± 11.5 | 71.1 ± 11.2 | <0.001 |
| **Physical Domain Score** | 42.7 ± 20.3 | 85.6 ± 19.4 | <0.001 | 42.4 ± 17.9 | 84.2 ± 19.9 | <0.001 |
| **Social Domain Score** | 33.5 ± 18.4 | 78.6 ± 16.5 | <0.001 | 32.9 ± 18.2 | 77.6 ± 16.7 | <0.001 |
| **Overall QOL Score** | 22.5 ± 11.6 | 68.8 ± 19.9 | <0.001 | 22.6 ± 13.0 | 68.6 ± 18.6 | <0.001 |

**Table 5:** Quality of life analysis

### Survival Outcomes

The median follow-up duration ranged from 6.0 to 21.0 months.

Median overall survival was 4.0 months (95% CI: 2.7–5.3) in Arm A compared with 3.5 months (95% CI: 1.3–4.6) in Arm B as illustrated in Table 6. Although a trend toward improved survival was observed in the Quad Shot arm, the difference did not reach statistical significance (log-rank $p=0.284$). Kaplan–Meier survival analysis is depicted in Figure 4 .

| Treatment Arm | Median overall survival (months) | 95% CI | p-value |
|---|---|---|---|
| Arm A | 4.0 | 2.7–5.3 | 0.284 |
| Arm B | 3.5 | 1.3–4.6 | 0.284 |

**Table 6.** Overall survival outcomes

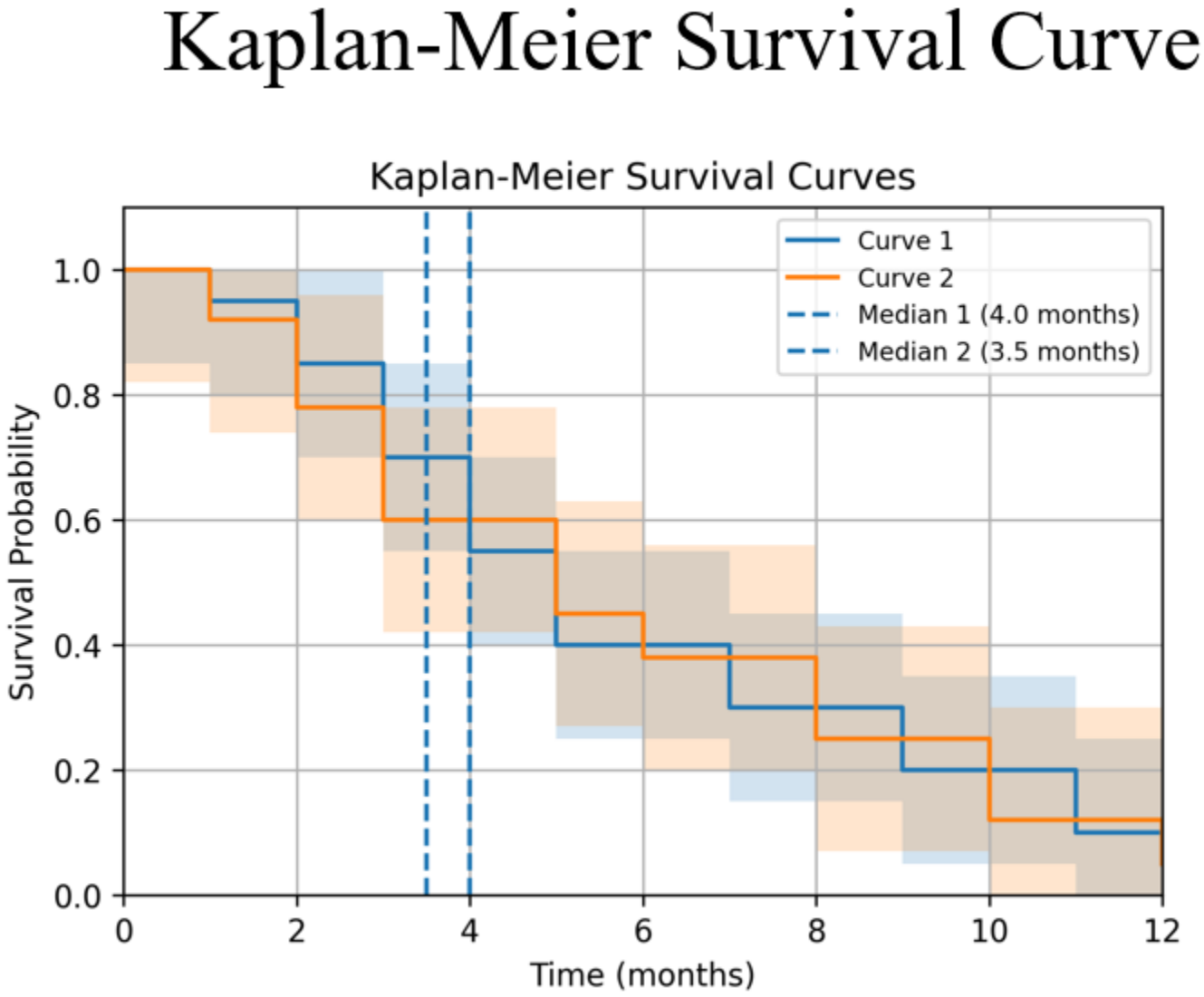


**Figure 4.** Kaplan–Meier overall survival curves comparing the two treatment arms along with number-at-risk table

## Discussion

Management of incurable locally advanced head and neck squamous cell carcinoma continues to be challenging in routine oncology practice, particularly in countries with high disease burden and limited healthcare resources. Many patients present with extensive locoregional disease accompanied by malnutrition, compromised airway or swallowing function, severe pain, and poor performance status, making curative treatment impractical. In such circumstances, the principal goals of treatment shift toward symptom reduction, preservation of dignity, maintenance of functional capacity, and improvement of patient comfort.

Hypofractionated palliative radiotherapy schedules are increasingly utilized because they allow rapid symptom control with fewer treatment visits and reduced interruption to supportive care. These schedules are especially valuable in frail patients who may not tolerate prolonged treatment courses. The present prospective randomized study compared two commonly used hypofractionated regimens and demonstrated that both approaches achieved meaningful palliation with acceptable acute toxicity.

The demographic and clinicopathological characteristics observed in the present study were comparable with previously published Indian and international studies evaluating palliative radiotherapy in advanced head and neck cancers. Male predominance and the high prevalence of tobacco-related habits observed in our study reflect the established epidemiological profile of head and neck cancers in the Indian population.

Treatment adherence was numerically superior in the Quad Shot arm compared with the short-course hypofractionated schedule. Improved compliance in the Quad Shot group may be attributable to the shorter cyclical treatment delivery, reduced uninterrupted treatment burden, and better patient tolerance. Similar observations regarding feasibility and patient acceptability of the Quad Shot approach have been described in previous palliative radiotherapy studies involving advanced head and neck cancers.

Both treatment regimens produced high rates of objective clinical response. More than 95% of evaluable patients in each arm demonstrated partial response following treatment completion, indicating comparable palliative efficacy between the two schedules. Earlier studies evaluating

hypofractionated radiotherapy in advanced head and neck malignancies have likewise reported rapid symptomatic improvement and encouraging local disease control using abbreviated treatment schedules.

Performance status improved significantly following treatment in both study arms. Improvement in Karnofsky Performance Status after palliative radiotherapy has also been reported in earlier studies and is clinically relevant because better functional status may improve oral intake, reduce caregiver dependence, and facilitate further supportive or systemic therapy.

Meaningful improvement in patient-reported quality-of-life outcomes was observed after treatment in both study groups. Domains related to pain relief, swallowing, mood, social interaction, and daily activity showed substantial post-treatment improvement. These findings support the role of palliative radiotherapy not only in tumor control but also in restoration of functional well-being and psychosocial comfort. The relatively favorable compliance observed with the Quad Shot regimen may additionally have contributed to sustained symptom relief.

Acute treatment-related adverse effects remained manageable in both treatment arms. Most patients developed only mild-to-moderate mucosal and skin reactions that responded adequately to conservative supportive measures. Severe mucositis was uncommon and no treatment-related mortality occurred. These findings further support the practical feasibility of hypofractionated palliative radiotherapy even among patients with compromised nutritional and functional status.

Median overall survival was 4.0 months in the Quad Shot arm and 3.5 months in the short-course hypofractionated arm. Although the difference was not statistically significant, a modest survival advantage was observed with the Quad Shot regimen. Previous studies evaluating palliative radiotherapy in advanced head and neck cancers have reported median survival durations ranging from approximately 3 to 6 months depending on baseline disease burden, nutritional status, and subsequent systemic therapy.

The present study has certain limitations. It was conducted at a single institution with a relatively small sample size and limited follow-up duration. In addition, radiological response assessment could not be uniformly performed in all patients because of logistical and financial constraints. Nevertheless, the prospective randomized design and inclusion of quality-of-life assessment strengthen the clinical relevance of the study.

Taken together, the findings of the present study suggest that both hypofractionated schedules are clinically effective options for palliation in incurable LAHNSCC. However, the Quad Shot regimen demonstrated relatively better treatment adherence along with a modest improvement in survival outcomes, supporting its utility as a pragmatic and patient-friendly approach in high-volume oncology centers and resource-limited settings.

## Conclusion

Both the Quad Shot regimen and short-course hypofractionated radiotherapy provided effective symptom palliation with acceptable toxicity in patients with incurable locally advanced head and neck squamous cell carcinoma. Both schedules achieved high clinical response rates with significant improvement in performance status and quality of life.

The Quad Shot regimen demonstrated comparatively better treatment compliance, favorable tolerability, and modest survival benefit, supporting its practical applicability in frail patients and resource-constrained settings. These findings reinforce the role of hypofractionated palliative radiotherapy as an effective and feasible approach for symptom control in advanced incurable head and neck cancers.

Further multicentric studies with larger sample sizes and integration of modern radiotherapy techniques and systemic therapies are warranted to optimize palliative treatment strategies in this patient population.

## Financial Support and Sponsorship

Nil.

## Conflicts of Interest

The authors declare no conflicts of interest.

## Acknowledgments

The authors sincerely acknowledge the support provided by the faculty, residents, nursing staff, radiation technologists, and supportive care teams of the Department of Radiation Oncology for their assistance during patient management and data collection throughout the study period.

The authors are also grateful to all the patients and their caregivers who participated in the study despite challenging clinical circumstances.

## References

1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, *et al*. (2021). Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin*; 71:209-249.
2. Bray F, Laversanne M, Weiderpass E, Soerjomataram I. (2021). The ever-increasing importance of cancer as a leading cause of premature death worldwide. *Cancer* 127:3029-3030.
3. Johnson DE, Burtness B, Leemans CR, Lui VWY, Bauman JE. et al. (2020). Head and neck squamous cell carcinoma. *Nat Rev Dis Primers*; 6:92.
4. Mathur P, Sathishkumar K, Chaturvedi M, Das P, Sudarshan KL, *et al*. (2020). Cancer statistics, 2020: Report from National Cancer Registry Programme, India. *JCO Glob Oncol;* 6:1063-1075.
5. Chauhan A, Koochakzadeh S, Sahu A, Locke J, Zender C. (2021). Management of advanced head and neck cancer in resource-limited settings. *Curr Opin Otolaryngol Head Neck Surg*; 29:107-114.
6. Grewal AS, Liu SCT. (2024). Palliative radiotherapy in the head and neck. Clin Oncol (R Coll Radiol); 36:114-123.
7. Crompton DJ, Mohammadi H, Wear MA, Wert KM, Barton MB. (2023). The role of Quad Shot in palliative radiotherapy for advanced head and neck cancer: A narrative review. *Ann Palliat Med*; 12:2211-2220.
8. Prakash S, Chakrabarti D, Kumar R, Agrawal MM, Chaturvedi A, Kumar N, *et al*. (2022). Palliative radiotherapy: A one-week course in advanced head and neck cancer-quality of life outcomes. *BMJ Support Palliat Care*;12:e192-e198.
9. Ghoshal S, Patel F, Mudgil N, Bansal AK, Sharma SC. (2019). Palliative radiotherapy in locally advanced head and neck cancer: A phase II study. *Indian J Palliat Care*; 25:95-101.

10. Soni A, Sharma DK, Singh AK, Kumar S, Goyal S. (2021). Comparative evaluation of hypofractionated palliative radiotherapy schedules in locally advanced head and neck cancers. *South Asian J Cancer*; 10:45-50.
11. Mudgal S, Chakraborty S, Gupta T, Laskar SG, Agarwal JP. (2020). Hypofractionated palliative radiotherapy in locally advanced head and neck cancer: Clinical outcomes and quality of life analysis. *Indian J Cancer*; 57:281-287.
12. Upadhyay R, Gogineni E, Tocaj G, Ma SJ, Bonomi M, *et al*. (2024). Palliative Quad Shot radiation therapy with or without concurrent immune checkpoint inhibition for head and neck cancer. *Cancers (Basel);* 16:1049.
13. Toya R, Fukugawa Y, Saito T, Matsuyama T, Yoshida R, *et al*. (2024). Radiation Therapy Oncology Group 8502 "QUAD shot" regimen using volumetric modulated arc therapy for incurable head and neck cancer. *Oral Oncol*; 151:106752.
14. (2025). Quad Shot-A tertiary hospital experience with a palliative radiotherapy regimen for head and neck cancer. *Clin Case Rep*;13: e70012.
15. Cabezas-Camarero S, Vazquez Masedo G, Puebla-Diaz F, Corona JA, Perez-Segura P. (2024). Major and durable responses to photon and electron-beam palliative radiotherapies after immune-checkpoint inhibitors in head and neck cancer. *Oral Oncol*; 150:106719.
16. Edge SB, Byrd DR, Compton CC, Fritz AG, Greene FL. et al. (2017). AJCC Cancer Staging Manual. 8th ed. New York: *Springer*.
17. Puraiya S, Kumar J, Yadav AK, Zaidi AK, Kumar R. et al. (2024). Comparison of conventional palliative radiotherapy fractionation schedule with Quad Shot regimen in locally advanced head and neck cancer patients: A randomised clinical trial. *J Clin Diagn Res;*18: XC01-7.
18. Saito T, Toya R, Fukugawa Y, Matsuyama T, Yoshida R, *et al*. (2024). Radiation Therapy Oncology Group 8502 "QUAD shot" regimen using volumetric modulated arc radiotherapy for incurable head and neck cancer. *Int J Radiat Oncol Biol Phys* [abstract]; 120: e281.
19. (2024). A phase II study of personalized ultrafractionated stereotactic adaptive radiotherapy for palliative head and neck cancer treatment (PULS-Pal): A single-arm clinical trial protocol. *BMC Cancer;* 24:1564.
20. Al-Mamgani A, Verhoef CG, Navran A, et al. (2020). Randomized controlled trial evaluating optimal palliative radiotherapy schedules in incurable head and neck squamous cell carcinoma. *Radiother Oncol*; 148:226-232.
21. Iqbal MS, Kelly C, Kovarik J, et al. (2020). Palliative radiotherapy for locally advanced non-metastatic head and neck cancer: A systematic review. *Radiother Oncol*; 148:70-80.
22. Ferro M, Macchia G, Re A, et al. (2021). Short-course accelerated radiotherapy in elderly patients with advanced head and neck cancer. *J Geriatr Oncol*; 12:987-993.
23. Bettazzi B, Salvestrini V, Banini M, et al. Sequencing immunotherapy and hypofractionated radiotherapy in frail patients with locally advanced head and neck squamous cell carcinoma.

## Putting In Perspective

### Central question

- Whether Quad Shot radiotherapy provides superior palliation and quality-of-life improvement compared with short-course hypofractionated radiotherapy in incurable locally advanced head and neck squamous cell carcinoma?
- Lack of prospective comparative Indian data evaluating commonly used palliative hypofractionated radiotherapy schedules.

### Key findings

- Partial response achieved in >95% patients in both treatment arms.
- Treatment compliance higher with Quad Shot regimen (80.0% vs. 71.4%).
- Significant improvement in Karnofsky Performance Status and UWQOL scores after treatment.
- Minimal Grade 3 toxicity observed with both regimens.
- Median overall survival 4.0 months with Quad Shot versus 3.5 months with short-course hypofractionated radiotherapy.

### Impact

- Quad Shot regimen provides effective palliation with acceptable toxicity in incurable LAHNSCC.
- Practical and feasible palliative radiotherapy approach for Indian patients in resource-constrained and high-volume oncology settings



DOI:10.31579/2690-4861/1144