Invitation of quotation

From

Interested national insurance agencies for providing clinical trials insurance.

At

All India Institute of Medical Sciences, Jodhpur

Inquiry No.	:	AIIMS/Admin/RES/133(II)/2024
Inquiry Issue Date	:	13 June 2024
Last Date of Submission	:	20 June 2024 at 03:00 PM.

All India Institute of Medical Sciences, Jodhpur

Basni Phase - II, Jodhpur – 342005, Rajasthan

Telefax: 0297- 2740741, Extn. 3109, email: **Procurement@aiimsjodhpur.edu.in**

www.aiimsjodhpur.edu.in

Invitation of quotation
From
Interested national insurance agencies for providing clinical trials insurance.
at, AIIMS Jodhpur

Sealed Quotations are hereby invited by the undersigned on behalf of the Dean (Research) AIIMS Jodhpur for the Institute as per terms & conditions mentioned below. The filled quotations along with all the required documents must reach in the office of the undersigned on or before 20/06/2024 03.00 PM. The Envelope containing the quotation would please be sealed and super scribed as under:-

"QUOTATION FROM INTERESTED NATIONAL INSURANCE AGENCIES FOR PROVIDING CLINICAL TRIALS INSURANCE AGAINST INQUIRY NO. AIIMS/ADMIN/RES/133(II)/2024" DUE ON 20/06/2024 03.00 PM"

1. Terms & Conditions:

A) The quotations received after this deadline & unsealed shall not be entertained under any circumstances whatsoever. In case of postal delay this Institute will not be responsible. **The offer Submitted Fax/Email shall not be considered, and no correspondence will be entertained in this matter.**

B) Quotations must be in the enclosed prescribed Performa on the letter head of the firm duly signed by the Proprietor/ Partner/Director or their authorized representative, in case of signing of quotation by the authorized representative letter of authorization must be attached with the quotation. Quotation must be dropped in "**Quotation Box**" located in Administration Block of AIIMS, Jodhpur.

C) Rates must be quoted in **Indian rupees** and as per the format specified taxes extra if any must be written separately.

D) No overwriting or cutting is permitted in the rate. If found, the quotation shall be summarily rejected.

E) The rates quoted must be valid for 60 days minimum from the date of opening of the quotation and silence of any tendered on this issue shall be treated as agreed with this condition.

F) Becoming L1 will not be the criteria for awarding of purchase order unless the rates are reasonable & justified.

G) RTGS/NEFT details need to be furnished by the supplier with the quotation on the letter head of supplier/firm/agency.

H) The firm/agency may satisfy the following conditions and attach self-attested copy of the same with the quotation:
- Firm shall be registered with the Government of Rajasthan / Central Government.
- The firm shall have valid GST/Other taxes and IT PAN.
- ***The firm should not be black listed by any Govt. Agency/Dept.***

I) Quotations qualified by such vague and indefinite expressions such as “subject to prior confirmation”, “subject to immediate acceptance” etc. will be treated as vague offers and rejected accordingly. Any conditional quotation shall be rejected summarily.

J) **Delivery Period** – within 30 days from work order.

K) **Payment Terms:** Payment will be only after submission of all documents.

L) **Disputes: -**In the event of any dispute or disagreement arising between the contractors and any other department of AIIMS Jodhpur with regards to the interpretation of “Terms & Conditions” of this inquiry, the same shall be referred to the Dean (Research), AIIMS Jodhpur whose decision will be final and binding upon the contractor.

M) AIIMS, Jodhpur reserves the right to reject any quotation or part or the whole of inviting quotation process without assigning any reason. Decision of the Dean (Research), AIIMS, Jodhpur will be final in this regard.

N) The near relatives of employees of AIIMS, Jodhpur are prohibited from participation in this tender. The near relative for this purpose are defined as: (a) Members of a Hindu undivided Family. (b) Their spouses (c) The one related to the other in the manner as father, son(s), Son's wife (daughter-in-law), daughter(s) and daughter's husband (sons-in-law) brother (s) and brother's wife, sister(s) and sister's husband, brother(s)-in-law.

Dean (Research)

Encl.: Annexure 1 (Specification)
Annexure 2 (Format of price bid)

Annexure 1

CLINICAL TRIAL LIABILITY: INSURANCE PROPOSAL FORM

Details:

1. Protocol Details of the studies – Attached (Protocol v3.0 Feb 2024)
2. Total No. of Patients participating in the studies. – 350 participants in 7 centres in India (List attached)
3. Patient Consent Forms: Attached
4. Start & End Date: 01/05/2024 to 30/04/2025 (One Year); to be renewed on annual basis for maximum of three years.
5. Details of the Institute and PI:
   - Name: SurVIC Trial Collaborative, AIIMS Jodhpur
   - Address: Room No. 3099, Department of Surgical Oncology AIIMS Jodhpur- 342005
   - Description of Business/Institute: AIIMS Jodhpur is Autonomous institute under the act of parliament Medical Education and Research Institute (Govt. of India).
   - Date of establishment: 2012
6. Are all trials conducted in full accordance with-

Particulars	Response
Department of Health requirements with protocols Approved by an IEC?	Yes
Royal College of Physicians recommendations?	NA
Applicable Government Department or Medical Body Or Pharmaceutical Industry Body guidelines?	Yes
E.C. guidelines on Good Clinical Practice?	Yes
I.C.H. Harmonised Tripartite Guidelines?	Yes

7. Give details of serious adverse events during the last 5 years resulting in death, disease or illness (physical or mental) to research subjects, and any circumstances, which have given or might give rise to a claim against you: Mentioned in study protocol.

Dr. Dharma Ram Poonia
सह - आचार्य
Associate Professor
कैंसर शल्य चिकित्सा विभाग
Department of Surgical Oncology
अखिल भारतीय आयुर्विज्ञान संस्थान, जोधपुर
All India Institute of Medical Sciences, Jodhpur

8. Full description of Clinical Trials to be conducted: Attached

9. For each trial please attach a copy of:
   - PROTOCOL (or summary thereof): Attached
   - ETHICS COMMITTEE SUBMISSION: Attached
   - VOLUNTEER CONSENT FORMAND/OR PATIENT: Attached
   - CTRI Registration: Attached

10. INFORMATION (as appropriate)
   - ANY HOLD HARMLESS AGREEMENT/CONTRACT: Nil
   - INDEMNITIES WITH OTHER PARTIES: Nil
   - SUMMARYOFTRIALSPERFORMEDINTHELAST12MONTHS: Fresh Trial
   - SUMMARYOFTRIALSPLANNEDINTHENEXT12MONTHS: Fresh Trial

11. If trials overlap period, please include in both tables allocating the appropriate number of Research Subjects to each time scale. Not applicable

12. Please state Limits of Indemnity for which a quotation is required or local currency equivalent.
   - Per each Clinical trial Subject Rs.25 Lakh
   - Total Coverage Per Annum Rs.100 Lakh

Contact details of PI:

Dr. Dharma Ram Poonia

Associate Professor, Department of Surgical Oncology

Principle Investigator- SurVIC Trial

AIIMS Jodhpur

Phone: 9958654196/ Email: drdharmapoonia@gmail.com

Dr. Dharma Ram Poonia
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All India Institute of Medical Sciences, Jodhpur

Note – Prospective bidders can request all attached documents mentioned in Annexure-1 by sending an email to drdharmapoonia@gmail.com.

[On the letterhead of firm]

ANNEXURE "2"

PRICE BIDFORM

To,

Dean (Research),
AIIMS, Jodhpur.

Dear Sir,

1. I/We …..... Submitted the quotation for Enquiry No. **"QUOTATION FOR CLINICAL TRAIL INSURANCE AT AIIMS, JODHPUR AGAINST THE INQUIRY NO. AIIMS/ADMIN/RES/133(II)/2024"** due on 20/06/2024 03.00 PM for providing Clinical Trials Insurance I/We thoroughly examined, understood, and accepted terms & conditions given in the enquiry document, failing which my quotation will be rejected out rightly.
2. I/We hereby offer to supply at the following rates.
3.

S. No.	Description	Premium Exclusive of GST (INR)	GST/ Other Taxes	Total Premium Inclusive of GST (INR)
1	As per annexure 1			

Note: -

1. The policy document shall clearly indicate various rates, Sum-insured, Scope of coverage, Extensions, Inclusions, Exclusions, and terms & conditions in line with bidding documents.
2. The Bidder must submit the GSTIN Registration and PAN Card self-attested copy with the quotation otherwise quotation will be REJECTED.
3. The bidder must quote their quotation only in above said format on the letter of firm otherwise quotation will be REJECTED.
4. The premium quoted must cover all the risks and perils as mentioned in annexure-1 Scope of Insurance Coverage

Date_____

Place _____

(Name)_____

Name of Firm/Company/Agency_____

GSTIN No.: _____

Bank Name:- _____

Bank Account No.: _____

IFSC Code:- _____

Branch Name: _____

Phone No._____

Email:_____

(Signature of Authorized Person) _____

Seal:_____

DOCUMENT: 1 & DOCUMENT: 1a

TITLE:

Upfront Surgery Vs Induction Chemotherapy Followed By Surgery In Oral Cavity Squamous Cell Cancers With Advanced Nodal Disease (SurVIC Trial): A Phase 3 Multicentric Randomized Controlled Trial

Study Acronym- SurVIC Trial (**Sur**gery **V**s **I**nduction **C**hemotherapy in Oral Cavity Cancer)

v1.0 Date: 22.10.2023

v2.0 Date: 04.02.2024

All India Institute of Medical Sciences- Jodhpur

1. **Synopsis:**

Title	Upfront **Sur**gery **V**s **I**nduction **C**hemotherapy Followed By Surgery In Oral Cavity Squamous Cell Cancers With Advanced Nodal Disease (SurVIC Trial): A Phase 3 Multicentric Randomized Controlled Trial
Rationale and Knowledge gap	A majority of oral cancer patients in India present in the advanced stage hence tend to have poor oncological outcomes. Chemotherapy has been associated with improved oncological outcomes in various cancers but its role in oral cancer is not well defined in curative setting apart from radio sensitization. Attempted trials of neoadjuvant chemotherapy failed to show oncological advantage despite an excellent response rate, in part due to poor patient selection. Patients with a biologically aggressive disease are more likely to benefit, hence we intend to find out the oncological advantage of adding induction chemotherapy to oral squamous cell cancer with advanced nodal disease (N2-N3).
Novelty	Earlier studies suffered from their heterogeneous patient population- all head and neck subsites together and included a spectrum ranging from early- stage operable cases to inoperable cancer. Due to such patient selection, the intended results were never met. The current study is intended to study the role of chemotherapy in curable patients who are most likely to benefit (biologically aggressive and advanced stage of presentation).
Objective	Primary: ● To study the 2 year disease free survival by adding induction chemotherapy before surgery in patients of oral cancer with advanced nodal disease as compared to upfront surgery. Secondary: ● To assess treatment related outcomes between the treatment arms- Response rate; Treatment compliance; treatment related toxicity, postoperative complications and Quality of life. ● To study the overall survival at 2 years. ● Oral cancer tissue biobanking for future translational research.
Study population	Operable Oral cavity Squamous cell carcinoma with advanced nodal disease (N2-N3)
Study Design	Open label, Multi centric, randomized controlled trial with allocation ratio of 1:1
Study Sites	Leading Center: **AIIMS Jodhpur** Collaborating Centers: **1. AIIMS Bhubaneswar** **2. AIIMS Rishikesh**

	3. AIIMS Bathinda **4. King's George Medical University , Lucknow** **5. Shri Mahant Indiresh Hospital, Dehradun** **6. Geetanjali Medical College, Udaipur**
Sample Size	The primary end point is disease-free survival. In order to have 80% power to detect a hazard ratio of 0.67, using a two-sided significance level, a total of 184 events are needed. Assuming an accrual rate of 15 patients a month, 300 patients need to be recruited. The analysis of DFS will take place 32 months after the start of the trial. The follow-up of patients will continue for 5 years. The analysis of OS will be conducted when 184 deaths are observed.
Inclusion Criteria	Biopsy proven, operable oral Squamous cell carcinoma cT1-T4; cN2-N3, with adequate organ function, Age- 18-75 years, ECOG-PS:0-2
Treatment Arms	**Standard Arm (SURG arm):** Surgery (Wide local Excision/composite resection with neck dissection) followed by adjuvant Radiotherapy ± Concurrent Chemotherapy **Experimental Arm (ICT):** 2# TPF based induction chemotherapy followed by Surgery (Wide local Excision/composite resection with neck dissection) followed by adjuvant Radiotherapy ± Concurrent Chemotherapy
Study endpoints	Primary- Disease free survival Secondary- Overall survival/ Quality of life/ Toxicity of treatment/ Treatment tolerance
Study duration	1. Preparation/ site initiation/IEC clearances/ MOUs- 3 Months 2. Participants accrual- 24 Months 3. Follow up and trial completion report- 9 Months 4. Follow up for Overall survival- 24 Months
Feasibility	As per past institutional experience, we expect to enrol the desired number of cases in 2 years. The approximate number of case accrual per centre is as follows- ● AIIMS Jodhpur- 50/ year ● King's George Medical university Lucknow- 40 patients/ year ● AIIMS Bhubaneswar- 25 patients/ year ● AIIMS Rishikesh- 25 patients/ year ● AIIMS Bathinda- 20 patients/ year ● Shri Guru Ram Rai Institute of Medical and Health Sciences & Shri Mahant Indiresh Hospital, Dehradun- 20 patients/ year

	● Geetanjali Medical College, Udaipur- 20 patients/ year

Trial Schema:

TITLE: Upfront Surgery Vs Induction Chemotherapy Followed By Surgery In Oral Cavity Squamous Cell Cancers With Advanced Nodal Disease (SurVIC Trial): A Phase 3 Multicentric Randomized Controlled Trial

1. **Priority Area-** Under the domain of Non-communicable diseases; Oral Cancer
2. **Area of research:** Interventional, Randomized control trial
3. **Key words:**

Oral Cavity Cancer, Induction Chemotherapy, Head and Neck Cancer, Pathological response, squamous cell carcinoma

4. **Abbreviations**:

OSCC: Oral squamous cell carcinoma; ICT: Induction chemotherapy; CTRT: Concurrent chemo-radiotherapy; DFS: Disease Free Survival; ICT: Induction Chemotherapy; NACT: Neoadjuvant Chemotherapy; OS: Overall Survival; QOL: Quality of Life; pCR: Pathological complete response; ICF: Informed consent Form; PID: Patient Information Document; CFR: Case record form; DSMB: Data safety and management Board.

5. Problem statement:

Oral Cavity Squamous cell carcinoma (OSCC) is one of the leading cancers in India and the incidence is only rising . More than 60% of them seek treatment in an advanced stage of the disease in India [1]. The treatment options for these patients include surgery or concurrent chemo-radiation (CTRT) based on disease status. Current standard of care for patients with locally advanced oral cancers is surgery followed by adjuvant treatment but long term oncological outcomes are dismal. Despite advances in oncological care, survival outcomes have not improved as per expectations in oral cavity cancer. Induction chemotherapy (ICT) followed by response based adjuvant therapy is an active area of research. Chemotherapy has proven beneficial in head and neck cancers and is a well-established standard of care in concurrent settings but Induction chemotherapy (ICT) has been explored only with limited success. The rationale behind induction therapy is multifactorial i.e., biological selection, addressing micro-metastasis, ease of resection or organ preservation. It has been proven pivotal in various settings across oncological practice. Induction chemotherapy in head and neck cancer is under investigation since the last 30 years but no significant progress has been made due to disease & patient population heterogeneity, improper patient selection, varied chemotherapy regimens, with sub-standard control arms [2-3].

Induction chemotherapy in advanced, surgically inoperable oral cancers before radical CTRT have failed to improve the oncological outcomes. PARADIGM trial, which was a multicentric American trial initiated by Dana-Farber Cancer Institute, showed no survival difference of adding ICT before CTRT. The trial suffered from incomplete accrual and lack of power [4]. Similar conclusions were made by the Spanish TTCC Trial [5]. Another trial named DeCIDE trial from the University of Chicago aimed to study whether induction chemotherapy provided survival gain in patients with N2-N3 disease [6]. However, the study was not powered enough to

provide meaningful conclusions. The third important study was the French GORTEC trial- a large study which included N2b-N3 patients and compared IC with TPF followed by concurrent Cetuximab based RT vs CTRT with Carboplatin-5FU [7]. This study used an inferior control arm and failed to show any differences in PFS or OS. However, they reported better distant metastasis free survival in the IC arm. Italian GSTTC Trial, though showed an overall survival and progression free survival improvement, the control arm received a non-standard treatment [8]. Meta-analysis by Zhang et al analysed 5 RCTs includes the mentioned above consisting of more than 900 patients and concluded that there is no benefit of adding IC before concurrent CTRT in locally advanced head and neck cancer in terms of overall survival, progression free survival, overall response rate and loco-regional recurrence; rather it increased the risk of grade 3-4 febrile neutropenia [9]. However the rate of pathological complete response and distant metastasis free survival was better with IC. ICT followed by CTRT based studies included patients from all the head and neck subset. If we look into the largest of the trials- the TTCC trial, it included only 93/ 439 patients across three arms [5]. Oral cavity cancer constituted only around 15-20% of the total study population, raising a concern on the generalizability. The chemotherapy regimen was also varied. The DeCIDE Trial used Hydroxyurea, while the GORTEC used Carboplatin. The control arms were inferior in GORTEC and the GSTTC trial. PARADIGM and the DeCIDE remain underpowered to study the OS and DFS due to poor accrual. Radiotherapy technique details were not reported and were variable. Oral cancer, when treated with nonsurgical management, are rarely curable. Hence, to study the role of ICT in oral cancer, the control arm must also be offered surgical management.

Detailed literature search on the role of ICT before surgery in OSCCs found- three published randomized controlled trials, one of which was by Licitra et al. in 2003 [10]. They included resectable T2-T4, any N oral cavity carcinomas and randomized them either to upfront surgery or cisplatin and 5-FU based chemotherapy. They did not find any survival benefit using induction chemotherapy. If we analyse the study in present context there are certain concerns to accept their results. Indication of RT has evolved post publication of this study after Bernier and Cooper's landmark work. Two drugs are inferior to triple agent based regimen. Moreover only 15% of the patients had advanced nodal disease (N2 or more) in their study. This study was closed prematurely due to poor accrual and they revised the power calculation. Long term follow-up published by Bossi et al concluded similar outcomes [11]. Another large RCT from China by Zhong et al included 256 resectable oral cavity cancer patients (T1-T4;N0-N2) and randomized them into upfront surgery vs one to two cycles of TPF based chemotherapy followed by surgery [12]. The authors reported that high risk patients did not receive concurrent chemotherapy with RT in interventional arm, which might have affected the control rate. On posthoc exploratory analysis they noted a survival benefit of using TPF in patient with N2 disease, though only 20% of their patients were N2 (OS hazard ratio- 0.418; 0.179-0.974 P- 0.043). [12-13]. Another prospective randomized trial from India by Tata Memorial, included the oral cavity cancer (T2-T4; Any N;M0) patients and randomized 34 patients each into upfront surgery vs 2 cycle of TPF based chemotherapy followed by surgery to study if NACT can improve the mandibular preservation rate. The study wasn't aimed or powered to study the survival outcomes. [14]

We propose to determine the role of induction chemotherapy in oral cavity cancer patients with an operable disease with advanced nodal stage (N2-N3). The hypothesis is derived from the Chinese study by Zhong

et al, where they have reported survival benefit in the subset of patients having advanced Nodal disease. Present study is a phase 3 randomized controlled trial aimed to determine the oncological outcome of adding ICT in the mentioned patient population.

6. **Rationale of the study:**

Oral cancer is still one of the most common cancers in India, 11.2% in men and 4.3% in women amongst all the cancer diagnosis. For various reasons like, lack of awareness, myths & superstitions, inaccessibility etc., most of them present late in a clinical setting. This not only subjects them to a myriad of treatment modalities spanning a significant time of treatment in the hospital setting, but also, often a very disfiguring and mutilating surgery. The standard of care for oral cancer SCC is surgery followed by adjuvant RT/CTRT or definitive CTRT in inoperable cases. The gray area of potential beneficiaries of the novel idea of induction chemotherapy followed by surgery and adj treatment, are a subset of patients with advanced nodal disease with increased disease burden, who can be given the said treatment, so as to make them amenable to not only a form preserving surgery, that may translate into reduced treatment related morbidity & rehabilitation needs, but also into oncological benefit in terms of disease free survival and subsequently overall survival. Most of the studies done previously are mainly retrospective in nature and having included all subsets of the head and neck region. We hereby attempt to conduct a prospective randomised controlled trial in order to evaluate the true benefit of induction chemotherapy in this particular subset of oral cancer patients with advanced nodal disease.

7. **Hypothesis:**

Induction chemotherapy in OSCC patients with advanced nodal disease (N2-N3) will improve the disease-free survival as compared to upfront surgery.

8. **Research Question:**

We would like to study if ICT followed by surgery improves the disease free interval in operable advanced nodal OSCC?

9. **Study Aim and Objectives**:

Aim:

- To study the impact of adding induction chemotherapy before surgery in patients of OSCC with advanced nodal disease compared to upfront surgery.

Objectives:

Primary:

- To study the 2 year disease free survival by adding induction chemotherapy before surgery in patients of oral cancer with advanced nodal disease as compared to upfront surgery.

Secondary:

- To assess treatment related outcomes between the treatment arms- Response rate; Treatment compliance; treatment related toxicity, postoperative complications and Quality of life.
- To study the overall survival at 2 years.
- Oral cancer tissue biobanking for future translational research.

10. Methodology:

10.1 . Study Design:

Open label, multi centric, Randomized controlled trial with allocation ratio of 1:1.

10.2. Study Site:

Leading site: All India Institute of Medical Sciences, Jodhpur (AIIMS-Jodhpur)

Collaborating sites:

- All India Institute of Medical Sciences, Rishikesh (AIIMS-R)
- All India Institute of Medical Sciences, Bathinda (AIIMS-BT)
- King's George Medical university, Lucknow (KGMU)
- All India Institute of Medical Sciences, Bhubaneshwar (AIIMS-Bh)
- Shri Mahant Indiresh Hospital, Dehradun (SMIH)
- Geetanjali Medical College, Udaipur (GMC)

10.3. Study Participants:

All biopsy/cytology-proven OSCC* presented to oncology outpatient departments will be considered for inclusion in the study after informed consent. Potential Participants will be screened for the eligibility criteria (mentioned below). The assessment of the eligibility will be done by surgeon, medical oncologist and radiation oncologist of the site (any two). All the participants will undergo detailed clinical, dental, nutritional evaluation, CECT/MRI Face & Neck, histopathological confirmation by incisional biopsy, ECG, 2D- Echocardiography and Routine haematology, biochemistry profile. Chest imaging is left to the discretion of the treating physician. Once participants get enrolled in the trial, they will be randomized in one the treatment arms.

Inclusion criteria

- Newly diagnosed, treatment naïve, biopsy or cytology proven OSCC
- Clinical Stage cT1-4a, cN2-N3**, M0- as per UICC 2018
- No evidence of distant metastases on chest x-ray and/or CT Thorax
- Age 18-75 years
- ECOG PS 0-2
- No contraindication to Cisplatin or radiotherapy***
- Patients eligible for definitive curative intent treatment after discussion in multidisciplinary tumour board
- Adequate organ function at time of participation, defined as
    - Haematological: Haemoglobin > 9gm/dl, ANC ≥ 1500/cmm3, Platelet ≥100000/cmm3
    - Liver Function test: Bilirubin ≤2 x upper limit normal (ULN), AST/ALT/ ALP ≤ 2.5 x ULN
    - Renal Function test: Creatinine ≤ 1.5 ULN, Creatinine Clearance ≥60 ml/min.

Exclusion criteria

- Pregnant.
- History of moderate to severe hearing loss.
- History of previous malignancy excluding non-melanoma skin cancers or cervical carcinoma in situ.
- Documented Weight loss of more than 15% in the last 6 months.
- Patients with known HIV, hepatitis B or C infection.

NOTE

**OSCC includes 'ICD 10th Edition- C02- C06' (Ref- UICC 8th Edition)- Buccal Mucosa, upper and lower Alveolus, hard palate, oral tongue, and floor of Mouth. Note: Lesions elsewhere including external lip (ICD 10th edition: C00.0/ C00.1 and C00.6: External Upper lip/ External Lower Lip/ Commissure) will not be included in the study.*

*** Criteria to define N2/N3*

Cross section imaging in the form of CECT or MRI of the face will be done or reviewed at the accrual centres. Nodal staging will be done using standard criteria of size, shape, central fatty hilum, relation with surrounding structures by radiologist. FNAC of the equivocal nodes will be done to establish the N Status. USG neck alone would suffice to label N stage, if clinician and radiologist are in consensus.

*** Contraindications for Cisplatin and Radiotherapy

ECOG Performance Status (PS) > 2, Renal failure, Neurologic abnormalities, Audiometric impairment, Hepatic, and Cardiovascular disease.

10.4. **Interventions- Control and Interventional arm**

Eligible Patients will be randomized to following treatment arms-

- SURG Arm= Control Arm: Upfront Surgery.
- ICT Arm= Experimental Arm: Induction Chemotherapy followed by surgery.

10.4.1. Details of intervention

Control Arm- SURG Arm

After initial evaluation for study eligibility, the participants of SURG arm will undergo the standard treatment, which is described below. Wide Local Excision (WLE) with 1cm, grossly normal tissue all around, including marked regions with or without involved bone with appropriate reconstruction. Unilateral or bilateral comprehensive neck dissection (Level I to V) based on the clinical indication as per description of operating surgeon. Margin adequacy can be assessed using frozen section or intra-operative gross examination based on discretion of the surgeon. Margin status reported on final paraffin block will be used to decide on adjuvant treatment. Surgical specimen will be analysed by the Onco-Pathologist of the participating institute. The final HPE will reported as per College of American Pathologist- Protocol for the Examination of Specimens from Patients with Cancers of the Oral Cavity version: 4.2.0.0/ June 2023 (Details in Histopathological assessment section). Adjuvant treatment after surgery will follow the indication as per National Comprehensive Cancer Network (NCCN) guidelines. Patients will receive Concurrent Cisplatin based CTRT if HPE shows margins or ENE+. All other patients with HPE showing any single adverse factor (pT3, pT4, close margin/perineural invasion/ Lympho-vascular invasion/more than one node positive/ positive node at level 4 or 5) will receive RT only. RT will be started

between 5-8 weeks post-surgery and will be delivered by IMRT with SIB or 3D CRT technique. Fitness for RT will be assessed by the operating surgeon and the radiation oncologist. Repeat dental, swallowing, nutritional and psychological assessment with counselling will be done (Annexure). CT imaging will be used for RT planning and dose dosimetry. The dose of the radiation- 66Gy (2Gy/fraction) to high-risk area and 50Gy (2Gy/fraction) to low-intermediate risk will be administered from Monday to Friday over 6 to 7 weeks with IMRT or 3D-CRT technique using linear accelerator (LINAC) with weekly Cisplatin (100mg/m2 every three week for 3 doses or 30 mg/m2 weekly) based concurrent chemotherapy that will be used as per the indication.

10.4.2. Experimental Arm: ICT Arm

Participants in the ICT arm will receive the treatment as follows. Participants will receive **2 Cycles of Induction chemotherapy** at 3 weekly intervals. The dose schedule (As per TAX 323)-

- Inj. Docetaxel 75mg/m2 IV Over 60 minutes Day-1;
- Inj. Cisplatin 75mg/m2 IV Over 60 minutes Over 60 minutes Day-1;
- Inj. 5 FU **750-1000mg/m2** IV Over 12 hours on Day1 to Day4 with GCSF/Peg-GCSF Support. $

NOTE:

$ Replacement of infusional 5FU with Tab. Capecitabine 850-1000mg/m^2 twice a day for 14 days in a three weekly cycle along with study protocol dosage of Taxane and Platinum, will be an acceptable option for the sites choosing the protocol for logistics reasons. [20-21]

Appropriate pre and post medications will be given. All patients will receive Peg-GCSG 6mg S/C prophylaxis 24 hours after chemotherapy and chemotherapy delays of up to two weeks or bone marrow recovery, whichever is earlier will be permitted. Chemotherapy toxicity assessment will be done and documented using Common Terminology Criteria for Adverse Effects (CTCAE v5.0). Chemotherapy dose modifications will be done by treating physicians according to grade of toxicity and treatment interruptions which will be recorded in CRF. Participants will receive high risk antiemetic prophylaxis as per NCCN guidelines. Study Participants having chemotherapy delays beyond 2 weeks will be discontinued from the ICT arm. Such participants will be considered for early surgical intervention or CTRT after recovery. Reductions in the dose of chemotherapy will be done in case of grade 4 chemotherapy toxicities. Neurotoxicity or ototoxicity of grade 3 or more will not be offered further ICT or CTRT. However, they will be considered for early surgery or radical RT.

Participants will undergo response assessment by clinical examination and Computed tomogram/PET CT using RECIST v1.1/ PERCISIT v1.1 at **3 weeks of completion of second cycle of ICT**. Patients with PR/CR or SD will go for surgical resection. Patients having PD but still localized and resectable will be offered surgical resection. If a patient progresses to become metastatic- palliative chemotherapy or appropriate palliative treatment will be offered. If surgically unresectable but still localized, definitive Radiotherapy with concurrent chemotherapy will be offered. Participants not consenting for surgery or deemed inoperable after ICT will be offered definitive CTRT and cause of inoperability will be documented. As we are planning **both intent to treat**

and per protocol analysis, all these patients will remain part of the study. Extent of the surgery and pathological assessment will be done as per the standard arm. Adjuvant treatment will be based on pre-treatment stage and HPE reports. In cases of complete pathological response, at least RT only be given. Positive margin and Extra nodal extension will be the indication for the Concurrent chemo-radiotherapy.

10.4.2a Histopathological assessment:

HPE:

Standard histopathological assessment will be done and recorded as per CAP guidelines version 4.2.0.0 June 2023. Post ICT case we don't have CAP or any validated guidelines for reporting. Based on our extensive search of literature and consensus amongst the pathologists of the institute we decide to use the 5 tier response recording system as given by Mandard et al (ref) which has been further validated by Hermann et al and Brucher et al. [17-19] it's based on the percentage of viable residual tumor cells and associated regressive changes. We will record data objective data on response in terms of residual viable tumour cells and regressive changes (fibrosis, inflammation and Necrosis) in terms of percentage. Stratification given by Mandard will used to data analysis which is as follows-

- complete regression (ypCR): only fibrosis with or without inflammation in tumor bed area, but no viable residual tumor cells.
- Subtotal regression (ypSR): presence of 10% viable residual tumor cells.
- Partial regression (ypPR): 10% to 50% viable residual tumor cells.
- minimal regression (ypMR): was characterized by 50% viable residual tumour cells.
- no change (ypNC): Absence of any regressive changes.

PCR: pCR was defined as having no residual invasive tumor in the primary surgical specimen and nodes removed following neoadjuvant therapy. Patients who had only in situ/ dysplasia will also considered to have a pCR.

IHC

IHC will be performed with p16 antibody and reporting will be as per CAP recommendation as follows-

- p16 positive: 70% or more nuclear and cytoplasmic expression with at least moderate to strong intensity either in primary or node).
- equivocal p16: 50-70% nuclear and cytoplasmic staining
- negative p16: less than 50%

Tumour Host Response Analysis: TIL, TAM and NK cells

The tumor-infiltrating lymphocytes (TILs) in the stromal compartment (stromal TILs) were assessed using the standardized methodology for TILs assessment described by the International TILs Working Group in

breast cancer by Salgado et al 9 and the International Immuno-oncology Biomarkers Working Group by Hendry et al 10.

TIL assessment on HPE:

Whole slide will be scanned at low magnification with ×5 or ×10 objective lens, followed by a higher magnification with ×20 objective lens. Stromal TILs defined as the percentage of stromal area occupied by infiltrating lymphocytes. The average number of TILs will assessed in multiple stromal areas. Mononuclear immune cells will scored, while polymorphonuclear leucocytes will be excluded. In addition, areas of necrosis too will be excluded. Furthermore, TILs in stromal areas not adjacent to the tumour will be excluded. Assessment of TILs will be carried out in areas of tumour growth in connective tissues. All available diagnostic slides stained with H-E will be evaluated. TILs will be assessed in percentages as a continuous score (5%, 10%, 20%, 30%... etc.).

Salivary Gland Invasion:

10.4.3. Criteria for discontinuation / modification

- Subject develops intolerable side effects
- Subject withdraws consent.
- Investigators believe that further continuation of therapy in a given patient will adversely affect the participants based on Interim analysis.****

10.5. Outcomes

Disease free survival will be calculated from the date of randomization to the date of clinical or pathological evidence of recurrence. Response assessment will be done using RECIST v1.1 if imaging performed. Clinical assessment of response will also be recorded. Overall survival will be calculated from the date of randomization to the date of death due to any reason. To assess the quality of life, we will use the FACT- HN scale. It will be analysed using the manual provided by FACIT.org. The quality of life questionnaire will be exercised at multiple points of time - Baseline, 3 month post treatment, 12 month post treatment, and 2 year post treatment. To assess the toxicity, Common Terminology Criteria for Adverse Events (CTCAE v5.0) will be used throughout the treatment duration. Postoperative complications will be assessed by Clavien-Dindo classification.

10.6 Sample size and feasibility

The primary end point is disease-free survival. For the sample size calculation we used time to event as outcome (disease free survival) and Hazard ratio as effect measure. Limited literature (only 2 trial- subset analysis and a meta-analysis) specifically looked into the hazard ratio in this setting. Reported hazard ratio for disease free survival in favour of ICT are- 0.55 to 0.71. [10-13] We kept the little conservative estimate

(HR-0.67) of benefit based on experience and consensus amongst our team of researchers. In order to have 80% power to detect a hazard ratio of 0.67, using a two-sided significance level, a total of 184 events are needed. Assuming an accrual rate of 15 patients a month, **a total of 300 patients need to be recruited**. The analysis of DFS will take place 32 months after the start of the trial. The follow-up of patients will continue for 5 years. The analysis of OS will be conducted when 184 deaths are observed.

As per past institutional experience, we expect to enrol the desired number of cases in 2 years. The approximate number of case accrual per centre is as follows-

Institute	Expected Year 1 Accrual	Expected Year 2 Accrual	All
AIIMS Jodhpur (JDH)	50	50	100
KGMU (LKO)	40	40	80
AIIMS Bhubaneswar (BBS)	25	25	50
AIIMS Rishikesh (RISHI)	25	25	50
AIIMS Bathinda (BTI)	20	20	40
Shri Mahant Indiresh Hospital, Dehradun (DDN)	20	20	40
Geetanjali Medical College, Udaipur (UDZ)	20	20	40
Total	200	200	400

Even with missing slow accrual at few centre, we should be enrol the subjects in desired time line taking the liberal estimate.

10.7. Implementational strategy:

10.7.1. Randomization and allocation concealment

Participants and treating clinician cannot be blinded due to obvious reasons. Data assessor will be blinded. Once a patient is found eligible, informed consent for the study will be taken. Patients would be randomized to one the treatment arm. Stratified block randomization will be done based on predefined strata using computer generated sequence. Stratification will be done based on Age of the patients (≤ 45 and >45)/ Subsite (Buccal mucosa-alveolar/ Tongue), and study centre.

Randomization will be done at the lead centre (AIIMS Jodhpur), when the enrolling personnel ensure the eligibility criteria and informed consent. Unique identification numbers will be generated and

allocation results will be communicated to the coordinator of the site by Email. Coordinator at AIIMS Jodhpur will reveal the treatment allocation to the treating physician.

10.7.2. Collaboration and coordination with other sites.

All the collaborating institutes will get the IEC clearance and MOU done at their own Institute. Draft of the MOU will be according to the rules laid down by the research section of AIIMS Jodhpur. Arrangement of logistics and manpower will be done in stipulated duration as mentioned in Gantt chart. Roles and SOP for each centre will be communicated. All the dependent and independent data will be collected at the individual centre. All collaborating centres will store the tissue for biobanking and send it to AIIMS Jodhpur. Tumour for biobanking will be stored at AIIMS Jodhpur.

10.7.3. Data collection and follow up duration

Data will be recorded prospectively in the predefined CRF. CRF will include the basic demographic information, clinical information, treatment information, and follow up information. CRF records will then be entered into the excel sheet/ redcap. Physical forms will be kept safe and secure. To ensure uniformity in the data collection and trial, training of the assessor from various centres will be done. Participants will be followed up every 3 monthly for the first year & every 6 monthly thereafter to collect the pertaining data. Patients will be followed up for overall survival data too, which would last up to death due to any reason or 3 years post treatment. OS data will be reported once predefined events occurred.

Before enrolment, all sites need to complete the IEC approvals and MOU signed. Data will be recorded prospectively in the predefined CRF. CRF will include the basic demographic information, clinical information, treatment information, and follow up information. CRF records will then be entered into the excel sheet/ redcap. Physical forms will be kept safe and secure. To ensure uniformity in the data collection and trial, training of the assessor from various centres will be done. Participants will be followed up every 3 monthly for the first year & every 6 monthly thereafter to collect the pertaining data. Patients will be followed up for overall survival data too, which would last up to death due to any reason or 3 years post treatment. OS data will be reported once predefined events occurred.

10.8. Definition of Study Endpoints

Disease free survival is defined as the **time from randomization to the time of the recurrence**, second primary, metastasis, relapse or death due to any cause. The duration of overall survival (OS) will be determined by measuring the time interval **from randomization to the date of death** or last observation (censored). Toxicity will be assessed using CTCAE criteria v5.

Quality of life assessment will be done using patient reported outcome questionnaires. We will use FACT scales- Functional Assessment of Cancer Therapy - General (FACT-G) and Head and Neck. It is a validated tool to study the quality of life of cancer patients [15-16]. Both English and Hindi language tools are available.

It includes four components- physical, social, emotional, and functional wellbeing. FACT H&N takes care of specific aspects of head and neck cancer. It contains 39 questions for 5 domains. Participants will be asked to fill the physical copy of the forms at various time frames- Baseline (Before induction chemotherapy will be additional assessment), before surgery, 3-months post treatment, 12-month post treatment, and 24-months post treatment. The data will be analysed using the methodology provided by FACIT. Financial toxicity assessment will be done using FACIT COST scale and Fatigue assessment will be done using FACIT Fatigue scale.

10.9. Participants safety:

10.9.1. Dose modification:

Dose modification will be done as per standard recommendations. Before starting chemotherapy patient status need to be assessed and ensured to have- No hematotoxicity of grade ≥2 ; No stomatitis, mucositis, diarrhoea, hand-foot syndrome, vomiting or other non- hematological toxicity beyond grade 1; No ongoing requirement for anti-diarrhoeal treatment; Bilirubin ≤ 2.0 x UNL and transaminases ≤ 5 x ULN; No evidence of cardiac toxicity; and ECOG PS0≥2. If any of these present, chemotherapy administration will be delayed until participants are free from these.

10.9.2. DCGI approval

This is an investigator-initiated study. No new or experimental medicines are planned to be used during this trial. As per gazette notification from the CDSCO, 'new drugs', DCGI approval is no longer needed; only an EC approval is required – 16th March, 2016 G.S.R. 313 (E)

10.9.3. Data monitoring:

Independent data monitoring committee (IDMC) will be constituted, having a team of surgeon, radiation oncologist, medical oncologist, statistician and patient advocate. IDMC will be independent of the funding agency and team of trial members. They monitor the study data every 6 months. Their recommendations will be followed.

10.9.3 Assessment of Adverse Events (AEs) and Serious Adverse Events (SAEs):

During each visit the investigator will evaluate the subject to determine whether any AEs/SAEs have occurred. AEs may be directly observed, reported spontaneously by the subject or by questioning the subject at each study visit. All laboratory values will be evaluated by the Investigator as to clinical significance. All post-baseline abnormal laboratory values considered clinically significant by the Investigator will be recorded as an AE. All clinical AEs occurring after the subject signs the Informed Consent From (ICF) and up to 30 days after the patient is taken off the active portion of the trial, whether observed by the investigator or reported by the subject, will be recorded as an AE.

Medical conditions that exist prior to the informed consent will be recorded as part of the medical history and will not be an AE. Diagnosis to be reported as the AE or SAE term; when the diagnosis is unavailable, signs and symptoms as individual entries of AE or SAE to be entered until the diagnosis becomes available. Pre-planned procedure/hospitalization for pre-existing conditions which do not worsen in severity would not be reported as SAEs.

Progressive disease is waived from SAE reporting. In addition, death due to progressive disease does not have to be reported as an SAE. The investigator would follow subjects with AEs until the event has resolved or the condition has stabilized. In case of an unresolved AEs including significant abnormal laboratory values at the end of treatment assessment, these events will be followed up until resolution or until they become clinically not relevant. The NCI Common Terminology Criteria for Adverse Events version 5 (NCI CTCAE v5.0) will be used to classify and grade the intensity of adverse events during and after each treatment cycle. CTCAE will be used to grade all events regardless of attribution, in order to ensure objective reporting, and in order to report trial data according to accepted international guidelines. The worst toxicity will be recorded. The results will be computed in a tabular form in which the proportion of people having their highest grade of toxicity will be charted.

10.9.4. Adverse Event

An ADVERSE EVENT (AE) is any untoward medical occurrence in a patient or clinical investigational subject administered a pharmaceutical product and which does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavourable or unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal investigational product, whether or not considered related to the medicinal product.

Adverse events include the following:

1. All suspected adverse drug or device reactions
2. Apparently unrelated illnesses, including the worsening (severity, frequency) of pre-existing illnesses
3. Injury or accidents.
4. Abnormalities in physiological testing or physical examination that require clinical intervention or further investigation (beyond ordering a repeat examination)
5. Laboratory abnormalities that require clinical intervention or further investigation (beyond ordering a laboratory test).
6. Any untoward event that occurs after the protocol-specified reporting period which the Investigator believes may be related to the drug or device.

7. AEs are not required to be reported unless they meet SAE criteria.

10.9.5. Serious adverse event (SAE)

SAE is any untoward medical occurrence that at any dose that results in

1. Death,
2. life-threatening (i.e. the subject is at risk of death at the time of the event),
3. requires inpatient hospitalization or prolongation of existing hospitalization,
4. Results in persistent or significant disability or incapacity,
5. Other important medical events which, in the opinion of the investigator, are likely to become serious if untreated, or as defined in the protocol
6. Significant overdose: In case of a significant overdose of a study drug, this has to be reported as a serious adverse event.

For the purposes of this study, the following adverse events are not reported as SAEs: Hospitalization or death as a result of or related to disease progression.

10.9.6. Procedure for reporting serious adverse events:

SAE reports will be forwarded to the IEC in the IEC approved format within 24 hours. collaborating centre would report SAE to AIIMS Jodhpur IEC within 7 days through Investigators.

10.9.7. Monitoring of subjects with adverse events

Any AE that occurs in the course of the clinical study must be monitored and followed up until the end of treatment visits. Patients would receive treatment as per institutional practice.

10.9.8. Compensation:

There is no provision of reimbursement for taking part in the study. Additional cost incurred due to AEs/SAEs will be borne by the treating institute.

10.9.9. Data Safety Monitoring Plan

Since this study has an intervention with potential for side effects, there will be a data safety monitoring committee which will be instituted which will periodically review the enrolment, and the side effects of the interventions etc. The members included for Data safety and monitoring Board (DSMB) will not be a part of the study protocol.

The constitution of the IDMC/DSMB will be as follows:

Total members -5

- Expert(s) in the clinical aspects of the disease/patient population being studied (4)- two experts from Surgical Oncology and two experts from Medical Oncology. One of the Experts will be selected as chairperson

- Biostatistician (1)

Frequency of Meeting: The committee will meet at least once in 6 months. Additional meetings may be called for any time a need arises depending on any serious adverse events which may happen during the conduct of the study. The chairman would call for the meeting and fix the time and place for the meeting.

Agenda: The agenda for the meeting would be to discuss the status of enrolment of the trial, the toxicities encountered up to the point. The investigators involved in the trial (PI or Co PI) will be expected to present the updates of the trial and also submit a 6-monthly update to the DSMB detailing the above issues.

The following items to be reviewed by the DSMB include:

1. Interim/cumulative data for evidence of study-related adverse events;
2. Interim/cumulative data for evidence of efficacy according to pre-established statistical guidelines, if appropriate;
3. Data quality, completeness, and timeliness;
4. Performance of individual centres;
5. Adequacy of compliance with goals for recruitment and retention, including those related to the participation of women and minorities;
6. Adherence to the protocol;

7. Factors that might affect the study outcome or compromise the confidentiality of the trial data (such as protocol violations, unmasking, etc.); and,

8. Factors external to the study such as scientific or therapeutic developments that may impact participant safety or the ethics of the study.

The DSMB should conclude each review with their recommendations to as to whether the study should continue without change, be modified, or be terminated. Recommendations regarding modification of the design and conduct of the study could include:

- Modifications of the study protocol based upon the review of the safety data;

- Suspension or early termination of the study because of serious concerns about subjects' safety, inadequate performance, or rate of enrolment.

- Suspension or early termination of the study because study objectives have been obtained according to pre-established statistical guidelines.

- Corrective actions regarding a study centre whose performance appears unsatisfactory or appears to raise questions regarding the conduct of the study.

Confidentiality will be maintained during all phases of DSMB review and deliberations. Usually, only voting members of the DSMB will have access to interim analyses of outcome data by treatment group. Exceptions may be made when the DSMB deems it appropriate. The reason and to whom the exceptions for access to interim analyses is granted will be documented in the Closed Session Report. DSMB members must maintain strict confidentiality concerning all privileged study results provided to them.

Reporting to the committee:

It would be the responsibility of the principal investigator to provide 6 monthly updates to the DSMB regarding the progress of recruitment, toxicities encountered etc. In addition to the routine updates done once in 6 months, the PI would also provide the DSMB with an email communication of any SAE or any other significant side effect which entails because of this study. This must be communicated within 24 hours by email and within 2 weeks a detailed report must be submitted.

Reports of the committee:

The committee would provide 6 monthly updates to the ethical committee regarding the progress of the trial with respect to any major safety issues noted. The committee would also provide recommendations to the EC regarding continuation of the study protocol. At any point, the committee can send a notice to the EC asking for suspending trial operations if the committee feels that the patient safety is endangered.

11.0. Stopping rules:

We don't plan any interim analysis. However, DSMB/IDMC will look into the data. In case of unexpected treatment related grade 5 toxicities of more than 5% and disease progression on ICT to make it surgical unresectable in more than 10% of the participants, we will consider to stop the trial.

12.0. Statistical analysis:

Categorical variables will be presented as frequency and percentage while Continuous variables will be expressed as mean/median with appropriate deviation measure based on skewness. Appropriate tests of significance will be used based on data nature. Survival data will be analysed using time to event analysis. HR

with 95% Confidence interval will be calculated by cox proportion hazard ration. HR will be compared using log rank and plotted using Kaplan- Meir curves. SPSS latest version will be used for data analysis.

13.1 Ethical issue:

The current trial is using the chemotherapy protocol already proven safe in different settings of OSCC. The study protocol will be presented in the Institute review board/ Institute ethical committee of the participating centres. After approval of the IRB/IEC, enrolment will begin. Appropriate patient insurances will be taken for the study participants for the study duration.

14.0. **Expected outcome/ deliverable aligned with research question**

Current study is a phase 3 randomized controlled trial to establish the superiority of ICT in OSCC with advanced nodal disease. It should provide new insights about the treatment armamentarium in this group of patients. It can be practice changing data for Indian patients, if we establish superiority. In case of negative trials, further futile exercise can be stopped.

15.0. **Future plan based on expected outcomes**

We will present our data at various scientific forums and publish it with journal of highest repute. We will develop a predictive and prognostic nomogram based on this moderate sized database. The bio banked oral cancer tissue will enable us to study basic tumorigenesis and it can facilitate further translational research using another research grant.

16.0. **Whether study will generate new intellectual property**

Present trial won't provide any new intellectual property. Proposed future studies should develop newer predictive nomogram will be produce IP. Our study will help the specific subset of patients with oral cancers who have higher neck disease burden. If on further follow up NACT in such patients translates into survival benefit (DFS/OS), this can be proposed as a new treatment guideline for future reference. As this project will be done in Western Indian region, where the disease burden in head & neck malignancies are high in the community, this project will provide representative insight into the treatment hypothesis. Should the proposed hypothesis stand true, using NACT will bridge the long waiting period of surgery for such cases who have a bulky operable disease, who otherwise may miss their chance of a curative surgery.

17.0. Timeline with achievable targets: GANTT/PERT chart

SURVIC Trial: GANTT Chart				
Activity	**Achievable milestones**	**Status**	**Duration**	**Cumulative duration**
Preparation	IEC/IRB approval & MOU- all sites		3 Months	0- 3M
	Arranging data collection software/Stationary			
	constitution of Independent data monitoring committee			
	Procurement of logistics and supplies			
	Staff Recruitment			
	Training of investigators and staff- Delegation log preparation			
	Site initiation			
	Dry run for screening and Acrual			
Patient accrual	Participants screening and accurals		24 Months	3M - 27M
	Procurement of logistics and supplies			
	Independent data monitoring committee visits			
	Safety review- Oversight by independent team			
	Data collection			
	Data review			
	End of accrual			
	Data of disease free survival		9 Months	27M-36M

Follow up data collection	Data analysis			
	Manuscript submission			
	Study completion report			
Follow up	Follow up for Overall survival		24 Months	36M- 60M
	Submission of Follow up Manuscript			

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भारतीय आयुर्विज्ञान अनुसंधान परिषद
स्वास्थ्य अनुसंधान विभाग, स्वास्थ्य एवं परिवार
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Dated: 29.01.2024

No.EM//Dev/SG/5887/2023/JJC
(E-office No. 175314)

To
The Registrar,
All India Institute of Medical Sciences,
Basni, Jodhpur,
Rajasthan 342005.

Sub: Sanction & Budget allotment of new Extramural Research (small-grants) Project entitled "***Upfront Surgery Vs Induction Chemotherapy Followed By Surgery In Oral Cavity Squamous Cell Cancers With Advanced Nodal Disease (SurVIC Trial): A Phase 3 Multicentric Randomized Controlled Trialunder*** under Dr. Dharma Ram Poonia, All India Institute of Medical Sciences, Basni, Jodhpur, Rajasthan 342005.

Sir

The Director General of the Council sanction the above mentioned research scheme initially for a period of one year from **01.02.2024 to 31.01.2025** subject to extension upto the total duration as mentioned below.

The Director General of the Council also sanctions the budget allotment of **Rs. 57,82,232/-** (Rupees Fifty Seven Lakhs Eighty Two Thousand Two Hundred and Thirty Two Only) as detailed in the attachment statement for the year 2023-24.

The grant in aid will be given subject to the following conditions:-

1. The payment of the grant will be release in installments to the Head of the Institute. The First Installment of the grant will be paid generally as soon as report regarding the commencement of the project and appointment of the staff is received by the Council.

2. The Staff appointed on the project should be paid as indicated in the budget statement attached.

3. The approved duration of the research scheme 3 **(Three) years**. The annual extension will be given after review of the work done on the research scheme during the previous years.

4. **The annual progress report** along with **Protocol** of work done be submitted to the Council every year after completion of ten months of the project. Failure to submit the report in time may lead to termination of the project.

5. The Institute will maintain a separate saving account of the receipts and expenditure incurred on the research scheme and will furnish a utilization certificate and an audited statement of the accounts pertaining to the grant along with interest thereon.

6. The host institute shall utilize the grant after following provision as laid down in *GFR-2017 and TA* rules.

7. The other terms & condition are available on ICMR website.

The receipt of this letter may please be acknowledged.

Yours faithfully,

(Harjeet Kaur Bajaj)
Administrative Officer

Accounts Section- V, ICMR-
(This issue with the concurrence of Finance Section vide E-office No. **175314** dated. 23.01.2024)

Copy to:-

1. Dr. Dharma Ram Poonia, All India Institute of Medical Sciences, Basni, Jodhpur, Rajasthan 342005.
2. EPMS ID-IIRP-2023-5887

Administrative Officer

INDIAN COUNCIL OF MEDICAL RESEARCH
ANSARI NAGAR, NEW DELHI-110029

Budget Statement for the 1st year duration
(From 01.02.2024 to 31.01.2025)

Sub:- "***Upfront Surgery Vs Induction Chemotherapy Followed By Surgery In Oral Cavity Squamous Cell Cancers With Advanced Nodal Disease (SurVIC Trial): A Phase 3 Multicentric Randomized Controlled Trialunder*** under Dr. Dharma Ram Poonia, All India Institute of Medical Sciences, Basni, Jodhpur, Rajasthan 342005.

Sl. No.	Particulars	1st year	Total
1.	**Staff**		
	Project Research Scientist –I (Non-Med.) @ Rs. 66,080/- in 1st year (including HRA 18%)	7,92,960/-	7,92,960/-
	Project Technical Support-III @ Rs. 33,040/- in 1st year (Number of post 7 for each sites)	27,75,360/-	27,75,360/-
	Total	**35,68,320/-**	**35,68,320/-**
2.	**Consumables**		
	Serum / tissue collection accessories	2,14,818/-	2,14,818/-
	Total	**2,14,818/-**	**2,14,818/-**
3.	**Contingency**		
	Patient Insurance	2,50,000/-	2,50,000/-
	Cloud space and data collection software's, stationary and other.	2,70,000/-	2,70,000/-
	Total	**5,20,000/-**	**5,20,000/-**
3.	Overhead Charges	1,29,094/-	1,29,094/-
4.	**Equipment**		
	Laboratory Deep Freeze 360-400 Litre-80 Degree	10,50,000/-	10,50,000/-
	Laptop/Desktop i9 or M3 chip	1,70,000/-	1,70,000/-
	SSD 2TBx2	30,000/-	30,000/-
	Total	**12,50,000/-**	**12,50,000/-**

5.	**Travel**		
	Travel Expenses	1,00,000/-	1,00,000/-
	Total	**1,00,000/-**	**1,00,000/-**
	Grand Total	**57,82,232/-**	**57,82,232/-**

(Rupees Fifty Seven Lakhs Eighty Two Thousand Two Hundred Thirty Two only)

Administrator Officer

INDIAN COUNCIL OF MEDICAL RESEARCH
Serving the nation since 1911

भारतीय आयुर्विज्ञान अनुसंधान परिषद
स्वास्थ्य अनुसंधान विभाग, स्वास्थ्य एवं परिवार कल्याण मंत्रालय, भारत सरकार

Indian Council of Medical Research
Department of Health Research, Ministry of Health and Family Welfare, Government of India

No.EM//Dev/SG/5887/2023/JJC ***Dated: 29.01.2024***
(E-office No. 175314)

Sub: Payment of full installment of 1st Year grant in aid for the research scheme entitled "***Upfront Surgery Vs Induction Chemotherapy Followed By Surgery In Oral Cavity Squamous Cell Cancers With Advanced Nodal Disease (SurVIC Trial): A Phase 3 Multicentric Randomized Controlled Trialunder*** under Dr. Dharma Ram Poonia, All India Institute of Medical Sciences, Basni, Jodhpur, Rajasthan 342005.

MEMORANDUM

The Director General, ICMR sanction the payment of **Rs. 57,82,232/- (Rupees Fifty Seven Lakhs Eighty Two Thousand Two Hundred and Thirty Two Only)** as the full installment of 1st Year grant for incurring expenditure in connection with the above mentioned research scheme. The amount of Rs. 57,82,232/- may be debited in the provision of Rs. 48,28,293/- made for the above research scheme for the current Financial Year 2023-24.

A formal bill for **Rs. 57,82,232/- is sent herewith for payment by RTGS to The Executive All India Institute of Medical Sciences, Basni, Jodhpur, Rajasthan 342005.**

(Harjeet Kaur Bajaj)
Admin. Officer

Accounts Section- V, ICMR-
(This issue with the concurrence of Finance Section vide E-office No. **175314** dated. 23.01.2024)

Copy to:
1. The Executive All India Institute of Medical Sciences, Basni, Jodhpur, Rajasthan 342005.
2. Dr. Dharma Ram Poonia, All India Institute of Medical Sciences, Basni, Jodhpur, Rajasthan 342005.
3. EPMS ID-IIRP-2023-5887

Administrative Officer

All India Institute of Medical Sciences, Jodhpur
Institutional Ethics Committee (Clinical Trial)

Registration No. ECR/866/Inst/RJ/2016/RR-19

No. AIIMS/IEC/2023/5784 Date: 17/10/2023

INSTITUTIONAL ETHICS COMMITTEE (CLINICAL TRIAL) APPROVAL CERTIFICATE

Certificate Reference Number: AIIMS/IEC/2023/4622

Project title: Upfront surgery Vs Indiction chemotherapy followed by surgery in oral cavity squamous cell cancers with advanced nodal disease (SurVIC Trial): A Phase 3 multicentric randomized controlled trial.

Nature of project: Extramural Multicentric Research Project

Dear Dr. Dharma Ram Poonia,

Your above-mentioned project was discussed in the Institutional Ethics Committee (Clinical Trial) meeting held on 13/10/2023. The meeting was attended by the following members:

1.	Dr. Praveen Sharma, Former Dean (Research), Professor & Head of Biochemistry, AIIMS, Jodhpur	Chairman
2.	Justice N.N. Mathur, Former Vice Chancellor, National Law University, Jodhpur	Member
3.	Dr. K.R. Haldiya, Former Scientist F, DMRC, Jodhpur	Member
4.	Dr. Kirti Rajimwale, Former Head, Dept. of Sociology, Jai Narain Vyas University, Jodhpur	Member
5.	Dr. Heera Ram, Associate Professor, Dept. of Zoology, Jai Narain Vyas University, Jodhpur	Member
6.	Dr. Pankaj Bhardwaj, Professor, Dept. of CM&FM, AIIMS, Jodhpur	Member
7.	Dr. Sumit Banerjee, Professor, Dept. of Orthopaedics, AIIMS, Jodhpur	Member
8.	Dr. Durga Shankar Meena, Assistant Professor, Dept. of General Medicine, AIIMS, Jodhpur	Member
9.	Dr. Jaykaran Charan, Additional Professor, Dept. of Pharmacology, AIIMS, Jodhpur	Member Secretary

We are pleased to inform you that your project has been approved with effect from the date of issuance of this letter.

- Principal Investigator and Co-Investigator must ensure that the study is conducted in compliance with the submitted protocol, GCP guidelines, The New Drugs & Clinical Trials Rules, 2019, ICMR National Ethical Guidelines and other aapplicable regulatory guidelines.
- This IEC approval is valid for the study period mentioned in the study protocol.
- Prior approval from the IEC is necessary for prolongation of study duration beyond the specified period.
- Any change/deviation from the protocol must be submitted to IEC with justification for the same, and should not be implemented without prior IEC approval.
- Any Serious Adverse Event during the study must be reported to IEC within 24 hours.
- PI must submit the progress report to the IEC for review at every six months, and the completion report at the completion of the study.
- IEC should be duly informed about any delay in starting the project or its premature termination, with justification for the same.

With Warm regards,

Yours Sincerely,

Dr. Jaykaran Charan
सदस्य सचिव
Member Secretary
संस्थागत नैतिकता समिति
Institutional Ethics Committee
अखिल भारतीय आयुर्विज्ञान संस्थान, जोधपुर
All India Institute of Medical Sciences, Jodhpur

Copy to: Dean (Research), AIIMS, Jodhpur

अखिल भारतीय आयुर्विज्ञान संस्थान, जोधपुर
संस्थागत नैतिकता समिति (नैदानिक परीक्षण)

पंजीकरण क्रमांकः ECR/866/Inst/RJ/2016/RR-19

सं. एम्स/आईईसी/2023/5784 दिनांकः 17.10.2023

संस्थागत नैतिकता समिति (नैदानिक परीक्षण) अनुमोदन प्रमाण पत्र

प्रमाणपत्र संदर्भ सं.: एम्स/आईईसी/2023/4622

प्रोजेक्ट का शीर्षकः Upfront surgery Vs Indiction chemotherapy followed by surgery in oral cavity squamous cell cancers with advanced nodal disease (SurVIC Trial): A Phase 3 multicentric randomized controlled trial.

प्रोजेक्ट की प्रकृतिः बाह्य अनुदानित बहुकेन्द्रीय अनुसंधान परियोजना

प्रिय डॉ. धर्माराम पूनिया,

आपके उपर्युक्त प्रोजेक्ट पर दिनांक 13.10.2023 को आयोजित संस्थागत नैतिकता समिति (नैदानिक परीक्षण) की बैठक में चर्चा की गई। बैठक में निम्नलिखित सदस्यों ने भाग लियाः

1.	डॉ. प्रवीण शर्मा, भूतपूर्व अधिष्ठाता (अनुसंधान), आचार्य एवं विभागाध्यक्ष, जैव रसायन विभाग, एम्स, जोधपुर	अध्यक्ष
2.	न्यायमूर्ति एन.एन माथुर, भूतपूर्व उपाध्यक्ष, राष्ट्रीय कानून विश्वविद्यालय, जोधपुर	सदस्य
3.	डॉ. के. आर. हल्दिया, पूर्व वैज्ञानिक एफ, डीएमआरसी, जोधपुर	सदस्य
4.	डॉ. कीर्ति राजिमवाले, पूर्व विभागाध्यक्ष, समाजशास्त्र विभाग, जय नारायण व्यास विश्वविद्यालय, जोधपुर	सदस्य
5.	डॉ. हीरा राम, सह–आचार्य, प्राणीशास्त्र विभाग, जय नारायण व्यास विश्वविद्यालय, जोधपुर	सदस्य
6.	डॉ. पंकज भारद्वाज, आचार्य, सामुदायिक चिकित्सा और परिवार चिकित्सा विभाग, एम्स, जोधपुर	सदस्य
7.	डॉ. सुमित बनर्जी, आचार्य, अस्थि रोग विभाग, एम्स, जोधपुर	सदस्य
8.	डॉ. दुर्गा शंकर मीना, सहायक आचार्य, जनरल मेडिसिन विभाग, एम्स, जोधपुर	सदस्य
9.	डॉ. जयकरण चारण, अतिरिक्त आचार्य, औषधी विज्ञान विभाग, एम्स, जोधपुर	सदस्य सचिव

हमें, आपको यह सूचित करते हुए हर्ष की अनुभूति हो रही है कि इस पत्र के जारी होने की तारीख से आपके प्रोजेक्ट को मंजूरी प्रदान कर दी गई है।

- प्रधान अन्वेषक एवं सह–अन्वेषक को यह सुनिश्चित करना चाहिए कि प्रस्तुत प्रोजेक्ट, जीसीपी दिशानिर्देशों, नई औषधि एवं नैदानिक परीक्षण नियम, 2019, आईसीएमआर राष्ट्रीय नैतिक दिशानिर्देशों और अन्य लागू नियामक दिशानिर्देशों की पालना करते हुये कार्यान्वयन किया जाये।
- यह संस्थागत आचार समिति (आईईसी) अनुमोदन प्रोजेक्ट में उल्लिखित अवधि के लिए मान्य है।
- निर्दिष्ट अवधि से आगे अध्ययन की अवधि बढाने के लिए संस्थागत आचार समिति (आईईसी) से पूर्व अनुमोदन आवश्यक है।
- प्रोटोकाल से कोई भी परिवर्तन संस्थागत आचार समिति (आईईसी) को उचित कारणों के साथ प्रस्तुत किया जाये, और आईईसी अनुमोदन के बिना परिवर्तन लागू नहीं किया जाये।
- अध्ययन के दौरान किसी भी गंभीर प्रतिकूल घटना की सूचना आईईसी को 24 घंटे के भीतर दी जाये।
- प्रधान अन्वेषक को प्रत्येक छह महीने में समीक्षा के लिए संस्थागत आचार समिति (आईईसी) को प्रगति रिपोर्ट और अध्ययन पूरा होने पर पूर्णता रिपोर्ट प्रस्तुत करनी होगी।
- संस्थागत आचार समिति (आईईसी) को उचित कारणों के साथ परियोजना शुरू करने में किसी भी देरी या समय से पहले समाप्ति के बारे में विधिवत सूचित किया जाये।

शुभकामनाएं

डॉ. जयकरण चारण
सदस्य सचिव
Member Secretary
संस्थागत नैतिकता समिति
Institutional Ethics Committee
अखिल भारतीय आयुर्विज्ञान संस्थान, जोधपुर
All India Institute of Medical Sciences, Jodhpur

प्रतिलिपिः डीन (अनुसंधान), एम्स, जोधपुर

FULL DETAILS (Read-only) -> Click Here to Create PDF for Current Dataset of Trial

CTRI No	**CTRI/2024/03/064586** [Registered on: 21/03/2024] **Trial Registered Prospectively**
Acknowledgement Number	REF/2024/01/077736
Last Modified On:	20/03/2024
Post Graduate Thesis	No
Type of Trial	Interventional
Type of Study	Drug
Study Design	Randomized, Parallel Group, Active Controlled Trial
Public Title of Study	Upfront Surgery Vs Induction Chemotherapy Followed By Surgery In Oral Cavity Squamous Cell Cancers
Scientific Title of Study	Upfront Surgery Vs Induction Chemotherapy Followed By Surgery In Oral Cavity Squamous Cell Cancers With Advanced Nodal Disease (SurVIC Trial): A Phase 3 Multicentric Randomized Controlled Trial
Trial Acronym	SurVIC Trial

Secondary IDs if Any

Secondary ID	Identifier
NIL	NIL

Details of Principal Investigator or overall Trial Coordinator (multi-center study)

Name	Dharma Ram Poonia
Designation	Associate Professor
Affliation	AIIMS Jodhpur
Address	Department of Surgical Oncology AIIMS Jodhpur SAme Jodhpur RAJASTHAN 342005 India
Phone	9958654196
Fax	
Email	drdharmapoonia@gmail.com

Details Contact Person Scientific Query

Name	Dharma Ram Poonia
Designation	Associate Professor
Affliation	AIIMS Jodhpur
Address	Department of Surgical Oncology AIIMS Jodhpur SAme RAJASTHAN 342005 India
Phone	9958654196
Fax	
Email	drdharmapoonia@gmail.com

Details Contact Person Public Query

Name	Dharma Ram Poonia
Designation	Associate Professor
Affliation	AIIMS Jodhpur
Address	Department of Surgical Oncology AIIMS Jodhpur SAme RAJASTHAN 342005 India
Phone	9958654196
Fax	
Email	drdharmapoonia@gmail.com

Source of Monetary or Material Support
Clarification(s) with Reply
Modification(s)

Indian council of Medical Research Small Grant

Primary Sponsor
Clarification(s) with Reply
Modification(s)

Name	Indian Council of Medical Research
Address	Indian Council of Medical Research New Delhi
Type of Sponsor	Government funding agency

Details of Secondary Sponsor

Name	Address
NIL	NIL

Countries of Recruitment

India

Sites of Study
Clarification(s) with Reply
Modification(s)

No of Sites = **7**

Name of Principal Investigator	Name of Site	Site Address	Phone/Fax/Email
Dr Rohit Mahajan	AIIMS Bathinda	Department of Radiation Oncology, AIIMS Bathinda Bathinda PUNJAB	9418400149 rohit.mahjn@gmail.com
Dr Dillip M	AIIMS Bubhaneswar	Department of Surgical Oncology, AIIMS Bhubaneshwar Khordha ORISSA	9013072969 dillipmuduly@gmail.com
Dr Dharma Ram Poonia	AIIMS Jodhpur	Department of Surgical Oncology Jodhpur Jodhpur RAJASTHAN	9958654196 drdharmapoonia@gmail.com
Dr Amit Sehrawat	AIIMS RIshikesh	Department of Medical Oncology,AIIMS Rishikesh Hardwar UTTARANCHAL	9958474477 dramitsehrawat@gmail.com
Dr Ashish J	Geetanjali Medical College, Udaipur	Department of Surgical Oncology, GMC Udaipur Udaipur RAJASTHAN	9868090607 ashish_jakhetiya@yahoo.com
Dr VIjay Kumar	KGMU Lucknow	Department of Surgical Oncology, KGMU, Lucknow Lucknow UTTAR PRADESH	9935383666 drvkumar2007@gmail.com
Dr Pankaj Garg	Shri Gutu Ram Rai Institute Health Sciences, Dehradun	Department of Surgical Oncology, SGRRIHS, Dehradun Dehradun UTTARANCHAL	9868708542 dr.pankajgarg@gmail.com

Details of Ethics Committee
Clarification(s) with Reply
Modification(s)

No of Ethics Committees= **7**

Name of Committee	Ethics Committee registered with DHR /CDSCO or not	Ethics Committee Registration No.	Approval Status	Date of Approval	Approval Document	Is IEC?
AIIMS Bathinda	Yes		Submittted/Under Review	No Date Specified		No
AIIMS Bhubhaneshwar	Yes		Submittted/Under Review	No Date Specified		No
AIIMS Rishikesh	Yes		Submittted/Under Review	No Date Specified		No
All India Institute of Medical Sciences, Jodhpur	No		Approved	17/10/2023	Approval File	No
Geetanjali Medical College Udiapur	Yes		Submittted/Under Review	No Date Specified		No
KGMU Lucknow	Yes		Submittted/Under Review	No Date Specified		No
Shri Gutu Ram Rai Institute & Health Sciences, Dehradun	Yes		Submittted/Under Review	No Date Specified		No

Regulatory Clearance Status from DCGI

Status	Date	Aproval Document
Not Applicable	No Date Specified	No File Uploaded

Health Condition / Problems Studied

Health Type	Condition
Patients	**(1) ICD-10 Condition:** C069||Malignant neoplasm of mouth, unspecified,

Intervention / Comparator Agent
Clarification(s) with Reply
Modification(s)

Type	Name	Details
Intervention	ICT arm	2 Cycle of chemotherapy followed by surgery 2 Cycles of Induction chemotherapy at 3 weekly intervals with the dose schedule- Inj. Docetaxel 75mg/m2 IV Over 60 minutes Day-1; Inj. Cisplatin 75mg/m2 IV Over 60 minutes Over 60 minutes Day-1; Inj. 5 FU 850-1000mg/m2 IV Over 12 hours on Day1 to Day4 with GCSF/Peg-GCSF Support. Replacement of infusional 5FU with Tab. Capecitabine 850-1000mg/m2 twice a day for 14 days in a three weekly cycle along with study protocol dosage of Taxane and Platinum, will be an acceptable option for the

			sites choosing the protocol for logistics reasons. Participants will undergo response assessment by clinical examination and Computed tomogram/PET CT using RECIST v1.1/ PERCISIT v1.1 at 3 weeks of completion of second cycle of ICT. Patients with PR/CR or SD will go for surgical resection. Patients having PD but still localized and resectable will be offered surgical resection. If a patient progresses to become metastatic- palliative chemotherapy or appropriate palliative treatment will be offered. If surgically unresectable but still localized, definitive Radiotherapy with concurrent chemotherapy will be offered. Participants not consenting for surgery or deemed inoperable after ICT will be offered definitive CTRT and cause of inoperability will be documented. As we are planning both intent to treat and per protocol analysis, all these patients will remain part of the study. Extent of the surgery and pathological assessment will be done as per the standard arm. Adjuvant treatment will be based on pre-treatment stage and HPE reports. In cases of complete pathological response, at least RT only be given. Positive margin and Extra nodal extension will be the indication for the Concurrent chemo-radiotherapy.
	Comparator Agent	SURG arm	Upfront surgery: After initial evaluation for study eligibility, the participants of SURG arm will undergo the standard treatment, which is described below. Wide Local Excision (WLE) with 1cm, grossly normal tissue all around, including marked regions with or without involved bone with appropriate reconstruction. Unilateral or bilateral comprehensive neck dissection (Level I to V) based on the clinical indication as per description of operating surgeon. Margin adequacy can be assessed using frozen section or intra-operative gross examination based on discretion of the surgeon. Margin status reported on final paraffin block will be used to decide on adjuvant treatment. Surgical specimen will be analysed by the Onco-Pathologist of the participating institute. The final HPE will reported as per College of American Pathologist- Protocol for the Examination of Specimens from Patients with Cancers of the Oral Cavity version: 4.2.0.0/ June 2023 (Details in Histopathological assessment section). Adjuvant treatment after surgery will follow the indication as per National Comprehensive Cancer Network (NCCN) guidelines. Patients will receive Concurrent Cisplatin based CTRT if HPE shows margins or ENE+. All other patients with HPE showing any single adverse factor (pT3, pT4, close margin/perineural invasion/ Lympho-vascular invasion/more than one node positive/ positive node at level 4 or 5) will receive RT only. RT will be started between 5-8 weeks post-surgery and will be delivered by IMRT with SIB or 3D CRT technique. Fitness for RT will be assessed by the operating surgeon and the radiation oncologist. Repeat dental, swallowing, nutritional and psychological assessment with counselling will be done (Annexure).Adjuvant treatmemnt as per standard guidelines

Inclusion Criteria

Age From	18.00 Year(s)
Age To	75.00 Year(s)
Gender	Both
Details	Biopsy proven, operable oral Squamous cell carcinoma cT1-T4; cN2-N3, with adequate organ function, Age- 18-75 years, ECOG-PS:0-2

Exclusion Criteria

Details	Pregnant, History of moderate to severe hearing loss, History of previous malignancy excluding non-melanoma skin cancers or cervical carcinoma in situ, Documented Weight loss of more than 15% in the last 6 months, or Patients with known HIV, hepatitis B or C infection.

Method of Generating Random Sequence

Computer generated randomization

Method of Concealment

Centralized

Blinding/Masking

Outcome Assessor Blinded

Primary Outcome
Clarification(s) with Reply
Modification(s)

Outcome	TimePoints
To study the 2 year disease free survival by adding induction chemotherapy before surgery in patients of oral cancer with advanced nodal disease as compared to upfront surgery.	2 Years

Secondary Outcome
Clarification(s) with Reply
Modification(s)

Outcome	TimePoints
To assess treatment related outcomes between the treatment arms- Response rate; Treatment compliance; treatment related toxicity, postoperative complications & Quality of life.	3 Months
To study the overall survival at 2 years.	2 Years
Oral cancer tissue biobanking for future translational research.	NA

Target Sample Size

Total Sample Size="300"
Sample Size from India="300"
Final Enrollment numbers achieved (Total)= "Applicable only for Completed/Terminated trials"
Final Enrollment numbers achieved (India)="Applicable only for Completed/Terminated trials"

Phase of Trial

Phase 3

Date of First Enrollment (India)

01/04/2024

Date of Study Completion (India)

Applicable only for Completed/Terminated trials

Date of First Enrollment

If country of recruitment is only India, global date would be not applicable.

(Global)	
Date of Study Completion (Global)	Applicable only for Completed/Terminated trials
Estimated Duration of Trial	**Years=**"3" **Months=**"0" **Days=**"0"
Recruitment Status of Trial (Global) Modification(s)	If country of recruitment is only India, global status would be not applicable.
Recruitment Status of Trial (India)	Not Yet Recruiting
Publication Details	N/A
Individual Participant Data (IPD) Sharing Statement	**Will individual participant data (IPD) be shared publicly (including data dictionaries)?** **Response** - YES 1. What data in particular will be shared? **Response** - Individual participant data that underlie the results reported in this article, after de-identification (text, tables, figures, and appendices). 2. What additional supporting information will be shared? **Response** - Study Protocol **Response** - Statistical Analysis Plan **Response** - Informed Consent Form **Response** - Clinical Study Report **Response** - Analytic Code 3. Who will be able to view these files? **Response** - Researchers who provide a methodologically sound proposal. 4. For what types of analyses will this data be available? **Response** - For individual participant data meta-analysis. 5. By what mechanism will data be made available? **Response (Others)** - drdharmapooni@gmail.com 6. For how long will this data be available *start date provided 01-04-2024 and end date provided 31-03-2029*? **Response** - Beginning 3 months and ending 5 years following article publication. 7. Any URL or additional information regarding plan/policy for sharing IPD? **Additional Information** - NIL
Result Disclosure	**Do you wish to upload results?** **Response** - Summary results have not yet been disclosed

Brief Summary

Title	Upfront **Sur**gery **V**s **I**nduction **C**hemotherapy Followed By Surgery In Oral Cavity Squamous Cell Cancers With Advanced Nodal Disease (SurVIC Trial): A Phase 3 Multicentric Randomized Controlled Trial
Rationale and Knowledge gap	Majority of oral cancers in India present in the advanced stage hence tend to have poor oncological outcomes. Chemotherapy has been associated with improved oncological outcomes in various cancers, but its role in oral cancer is still not well defined in curative settings, beyond radio sensitization. Attempted trials of Neoadjuvant chemotherapy failed to show oncological advantage despite an excellent response rate, in part due to poor patient selection. Patients with a biologically aggressive disease are more likely to benefit, hence we intend to find out the oncological advantage of adding induction chemotherapy to oral squamous cell cancer with advanced nodal disease (N2-N3).
Novelty	Earlier studies suffered from their heterogeneous patient population- all head and neck subsites together and included either inoperable cancer/ early-stage operable cases. Due to such patient selection, the intended results were never met. The current study is intended to study the role of chemotherapy in curable patients who are most likely to benefit (biologically aggressive and advanced stage of presentation).
Objective	Primary: • To study the 2 year disease free survival by adding induction chemotherapy before surgery in patients of oral cancer with advanced nodal disease as compared to upfront surgery.

	Secondary: • To assess treatment related outcomes between the treatment arms- Response rate; Treatment compliance; treatment related toxicity, postoperative complications and Quality of life. • To study the overall survival at 2 years. • Oral cancer tissue biobanking for future translational research.
Study population	Operable Oral cavity Squamous cell carcinoma with advanced nodal disease (N2-N3)
Study Design	Open label, Multi centric, randomized controlled trial with allocation ratio of 1:1
Study Sites	Leading Center: **AIIMS Jodhpur** Collaborating Centers: **1. AIIMS Bhubaneswar** **2. AIIMS Rishikesh** **3. AIIMS Bathinda** **4. King's George Medical university Lucknow** **5. Shri Mahant Indiresh Hospital, Dehradun** **6. Geetanjali Medical College, Udaipur**
Sample Size	The primary end point is disease-free survival. In order to have 80% power to detect a hazard ratio of 0.67, using a two-sided significance level, a total of 184 events are needed. Assuming an accrual rate of 15 patients a month, 300 patients need to be recruited. The analysis of DFS will take place 32 months after the start of the trial. The follow-up of patients will continue for 5 years. The analysis of OS will be conducted when 184 deaths are observed.
Inclusion Criteria	Biopsy proven, operable oral Squamous cell carcinoma cT1-T4; cN2-N3, with adequate organ function, Age- 18-75 years, ECOG-PS:0-2
Treatment Arms	**Standard Arm (SURG arm):** Surgery (Wide local Excision/composite resection with neck dissection) followed by adjuvant Radiotherapy ± Concurrent Chemotherapy **Experimental Arm (ICT):** 2# TPF based induction chemotherapy followed by Surgery (Wide local Excision/composite resection with neck dissection) followed by adjuvant Radiotherapy ± Concurrent Chemotherapy
Study endpoints	Primary- Disease free survival Secondary- Overall survival/ Quality of life/ Toxicity of treatment/ Treatment tolerance
Study duration	1. Preparation/ site initiation/IEC clearances/ MOUs- 3 Months 2. Participants accrual- 24 Months 3. Follow up and trial completion report- 9 Months 4. Follow up for Overall survival- 24 Months
Feasibility	As per past institutional experience, we expect to enrol the desired number of cases in 2 years. The approximate number of case accrual per centre is as follows- • AIIMS Jodhpur- 50/ year

- King’s George Medical university Lucknow- 40 patients/ year
- AIIMS Bhubaneswar- 25 patients/ year
- AIIMS Rishikesh- 25 patients/ year
- AIIMS Bathinda- 20 patients/ year
- Shri Guru Ram Rai Institute of medical and Health Sciences & Shri Mahant Indiresh Hospital, Dehradun- 20 patients/ year
- Geetanjali Medical College, Udaipur- 20 patients/ year

FULL DETAILS (Read-only) -> Click Here to Create PDF for Current Dataset of Trial

CTRI No	**CTRI/2024/03/064586** [Registered on: 21/03/2024] **Trial Registered Prospectively**
Acknowledgement Number	REF/2024/01/077736
Last Modified On:	20/03/2024
Post Graduate Thesis	No
Type of Trial	Interventional
Type of Study	Drug
Study Design	Randomized, Parallel Group, Active Controlled Trial
Public Title of Study	Upfront Surgery Vs Induction Chemotherapy Followed By Surgery In Oral Cavity Squamous Cell Cancers
Scientific Title of Study	Upfront Surgery Vs Induction Chemotherapy Followed By Surgery In Oral Cavity Squamous Cell Cancers With Advanced Nodal Disease (SurVIC Trial): A Phase 3 Multicentric Randomized Controlled Trial
Trial Acronym	SurVIC Trial

Secondary IDs if Any

Secondary ID	Identifier
NIL	NIL

Details of Principal Investigator or overall Trial Coordinator (multi-center study)

Name	Dharma Ram Poonia
Designation	Associate Professor
Affliation	AIIMS Jodhpur
Address	Department of Surgical Oncology AIIMS Jodhpur SAme Jodhpur RAJASTHAN 342005 India
Phone	9958654196
Fax	
Email	drdharmapoonia@gmail.com

Details Contact Person Scientific Query

Name	Dharma Ram Poonia
Designation	Associate Professor
Affliation	AIIMS Jodhpur
Address	Department of Surgical Oncology AIIMS Jodhpur SAme RAJASTHAN 342005 India
Phone	9958654196
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Affliation	AIIMS Jodhpur
Address	Department of Surgical Oncology AIIMS Jodhpur SAme RAJASTHAN 342005 India
Phone	9958654196
Fax	
Email	drdharmapoonia@gmail.com

Source of Monetary or Material Support
Clarification(s) with Reply
Modification(s)

Indian council of Medical Research Small Grant

Primary Sponsor
Clarification(s) with Reply
Modification(s)

Name	Indian Council of Medical Research
Address	Indian Council of Medical Research New Delhi
Type of Sponsor	Government funding agency

Details of Secondary Sponsor

Name	Address
NIL	NIL

Countries of Recruitment

India

Sites of Study
Clarification(s) with Reply
Modification(s)

No of Sites = **7**

Name of Principal Investigator	Name of Site	Site Address	Phone/Fax/Email
Dr Rohit Mahajan	AIIMS Bathinda	Department of Radiation Oncology, AIIMS Bathinda Bathinda PUNJAB	9418400149 rohit.mahjn@gmail.com
Dr Dillip M	AIIMS Bubhaneswar	Department of Surgical Oncology, AIIMS Bhubaneshwar Khordha ORISSA	9013072969 dillipmuduly@gmail.com
Dr Dharma Ram Poonia	AIIMS Jodhpur	Department of Surgical Oncology Jodhpur Jodhpur RAJASTHAN	9958654196 drdharmapoonia@gmail.com
Dr Amit Sehrawat	AIIMS RIshikesh	Department of Medical Oncology,AIIMS Rishikesh Hardwar UTTARANCHAL	9958474477 dramitsehrawat@gmail.com
Dr Ashish J	Geetanjali Medical College, Udaipur	Department of Surgical Oncology, GMC Udaipur Udaipur RAJASTHAN	9868090607 ashish_jakhetiya@yahoo.com
Dr VIjay Kumar	KGMU Lucknow	Department of Surgical Oncology, KGMU, Lucknow Lucknow UTTAR PRADESH	9935383666 drvkumar2007@gmail.com
Dr Pankaj Garg	Shri Gutu Ram Rai Institute Health Sciences, Dehradun	Department of Surgical Oncology, SGRRIHS, Dehradun Dehradun UTTARANCHAL	9868708542 dr.pankajgarg@gmail.com

Details of Ethics Committee
Clarification(s) with Reply
Modification(s)

No of Ethics Committees= **7**

Name of Committee	Ethics Committee registered with DHR /CDSCO or not	Ethics Committee Registration No.	Approval Status	Date of Approval	Approval Document	Is IEC?
AIIMS Bathinda	Yes		Submittted/Under Review	No Date Specified		No
AIIMS Bhubhaneshwar	Yes		Submittted/Under Review	No Date Specified		No
AIIMS Rishikesh	Yes		Submittted/Under Review	No Date Specified		No
All India Institute of Medical Sciences, Jodhpur	No		Approved	17/10/2023	Approval File	No
Geetanjali Medical College Udiapur	Yes		Submittted/Under Review	No Date Specified		No
KGMU Lucknow	Yes		Submittted/Under Review	No Date Specified		No
Shri Gutu Ram Rai Institute & Health Sciences, Dehradun	Yes		Submittted/Under Review	No Date Specified		No

Regulatory Clearance Status from DCGI

Status	Date	Aproval Document
Not Applicable	No Date Specified	No File Uploaded

Health Condition / Problems Studied

Health Type	Condition
Patients	**(1) ICD-10 Condition:** C069||Malignant neoplasm of mouth, unspecified,

Intervention / Comparator Agent
Clarification(s) with Reply
Modification(s)

Type	Name	Details
Intervention	ICT arm	2 Cycle of chemotherapy followed by surgery 2 Cycles of Induction chemotherapy at 3 weekly intervals with the dose schedule- Inj. Docetaxel 75mg/m2 IV Over 60 minutes Day-1; Inj. Cisplatin 75mg/m2 IV Over 60 minutes Over 60 minutes Day-1; Inj. 5 FU 850-1000mg/m2 IV Over 12 hours on Day1 to Day4 with GCSF/Peg-GCSF Support. Replacement of infusional 5FU with Tab. Capecitabine 850-1000mg/m2 twice a day for 14 days in a three weekly cycle along with study protocol dosage of Taxane and Platinum, will be an acceptable option for the

			sites choosing the protocol for logistics reasons. Participants will undergo response assessment by clinical examination and Computed tomogram/PET CT using RECIST v1.1/ PERCISIT v1.1 at 3 weeks of completion of second cycle of ICT. Patients with PR/CR or SD will go for surgical resection. Patients having PD but still localized and resectable will be offered surgical resection. If a patient progresses to become metastatic- palliative chemotherapy or appropriate palliative treatment will be offered. If surgically unresectable but still localized, definitive Radiotherapy with concurrent chemotherapy will be offered. Participants not consenting for surgery or deemed inoperable after ICT will be offered definitive CTRT and cause of inoperability will be documented. As we are planning both intent to treat and per protocol analysis, all these patients will remain part of the study. Extent of the surgery and pathological assessment will be done as per the standard arm. Adjuvant treatment will be based on pre-treatment stage and HPE reports. In cases of complete pathological response, at least RT only be given. Positive margin and Extra nodal extension will be the indication for the Concurrent chemo-radiotherapy.
	Comparator Agent	SURG arm	Upfront surgery: After initial evaluation for study eligibility, the participants of SURG arm will undergo the standard treatment, which is described below. Wide Local Excision (WLE) with 1cm, grossly normal tissue all around, including marked regions with or without involved bone with appropriate reconstruction. Unilateral or bilateral comprehensive neck dissection (Level I to V) based on the clinical indication as per description of operating surgeon. Margin adequacy can be assessed using frozen section or intra-operative gross examination based on discretion of the surgeon. Margin status reported on final paraffin block will be used to decide on adjuvant treatment. Surgical specimen will be analysed by the Onco-Pathologist of the participating institute. The final HPE will reported as per College of American Pathologist- Protocol for the Examination of Specimens from Patients with Cancers of the Oral Cavity version: 4.2.0.0/ June 2023 (Details in Histopathological assessment section). Adjuvant treatment after surgery will follow the indication as per National Comprehensive Cancer Network (NCCN) guidelines. Patients will receive Concurrent Cisplatin based CTRT if HPE shows margins or ENE+. All other patients with HPE showing any single adverse factor (pT3, pT4, close margin/perineural invasion/ Lympho-vascular invasion/more than one node positive/ positive node at level 4 or 5) will receive RT only. RT will be started between 5-8 weeks post-surgery and will be delivered by IMRT with SIB or 3D CRT technique. Fitness for RT will be assessed by the operating surgeon and the radiation oncologist. Repeat dental, swallowing, nutritional and psychological assessment with counselling will be done (Annexure).Adjuvant treatmemnt as per standard guidelines

Inclusion Criteria

Age From	18.00 Year(s)
Age To	75.00 Year(s)
Gender	Both
Details	Biopsy proven, operable oral Squamous cell carcinoma cT1-T4; cN2-N3, with adequate organ function, Age- 18-75 years, ECOG-PS:0-2

Exclusion Criteria

Details	Pregnant, History of moderate to severe hearing loss, History of previous malignancy excluding non-melanoma skin cancers or cervical carcinoma in situ, Documented Weight loss of more than 15% in the last 6 months, or Patients with known HIV, hepatitis B or C infection.

Method of Generating Random Sequence

Computer generated randomization

Method of Concealment

Centralized

Blinding/Masking

Outcome Assessor Blinded

Primary Outcome
Clarification(s) with Reply
Modification(s)

Outcome	TimePoints
To study the 2 year disease free survival by adding induction chemotherapy before surgery in patients of oral cancer with advanced nodal disease as compared to upfront surgery.	2 Years

Secondary Outcome
Clarification(s) with Reply
Modification(s)

Outcome	TimePoints
To assess treatment related outcomes between the treatment arms- Response rate; Treatment compliance; treatment related toxicity, postoperative complications & Quality of life.	3 Months
To study the overall survival at 2 years.	2 Years
Oral cancer tissue biobanking for future translational research.	NA

Target Sample Size

Total Sample Size="300"
Sample Size from India="300"
Final Enrollment numbers achieved (Total)= "Applicable only for Completed/Terminated trials"
Final Enrollment numbers achieved (India)="Applicable only for Completed/Terminated trials"

Phase of Trial

Phase 3

Date of First Enrollment (India)

01/04/2024

Date of Study Completion (India)

Applicable only for Completed/Terminated trials

Date of First Enrollment

If country of recruitment is only India, global date would be not applicable.

(Global)	
Date of Study Completion (Global)	Applicable only for Completed/Terminated trials
Estimated Duration of Trial	**Years=**"3" **Months=**"0" **Days=**"0"
Recruitment Status of Trial (Global) Modification(s)	If country of recruitment is only India, global status would be not applicable.
Recruitment Status of Trial (India)	Not Yet Recruiting
Publication Details	N/A
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"Upfront Surgery vs Induction Chemotherapy followed by surgery in Oral Cancers with advanced nodal disease (SurVIC Trial): A Randomized Controlled Trial"

SurVIC Trial

CASE RECORD FORM- CRF

Patient Name:	
Hospital CR Number:	
Trial ID	
Age/ Gender:	
Contact No. 1:	
Contact No. 2:	
Address:	
Treatment Arm	Surg Arm/ ICT Arm
Stratification	Age (≤ 45 or >45) (Buccal mucosa-alveolar or Tongue) Study Centre (C…….)

Note:

To be filled by trial coordinator when clinician refer them for possible enrollment.

PI/Co-I need to informed and should be invited during the counselling.

Screening:

Trial Number	

"SurVIC Trial"

S. No.	Inclusion Criteria	Yes	No
1	Age 18-75 years; ECOG PS 0-2		
2	Clinical Stage cT1-4a, cN2-N3*, M0- as per UICC 2018		
3	Newly diagnosed, treatment naïve, biopsy or cytology proven OSCC		
4	No contraindication to Cisplatin or radiotherapy**		
5	Patients eligible for definitive curative intent treatment after discussion in multidisciplinary tumour board		
6.	Adequate organ function at time of participation- • Haematological: Haemoglobin > 9gm/dl, ANC ≥ 1500/cmm3, Platelet ≥100000/cmm3 • Liver Function test: Bilirubin ≤2 x upper limit normal (ULN), AST/ALT/ ALP ≤ 2.5 x ULN Renal Function test: Creatinine ≤ 1.5 ULN, Creatinine Clearance ≥60 ml/min.		
Patients who meet *all of the inclusion criteria* are eligible for study. Please subject them for exclusion criteria.			
S. No.	Exclusion Criteria	Yes	No
1	Pregnant		
2	History of moderate to severe hearing loss.		
3	History of previous malignancy excluding non-melanoma skin cancers or cervical carcinoma in situ.		
4	Documented Weight loss of more than 15% in the last 6 months.		
5	Patients with known HIV, hepatitis B or C infection.		
If *all are "no"*, please, procced for informed consent. Otherwise record as screening failure			
Screening outcome : Eligible/ Fail			

* Ideally Cross section imaging in the form of CECT or MRI of the Face & Neck should be done or reviewed at the accrual centers. USG neck alone would suffice to label N stage if clinician believes so. Nodal staging will be done using standard criteria of size, shape, central fatty hilum, relation with surrounding structures by radiologist. FNAC of the equivocal nodes will be done to establish the N Status.

** ECOG Performance Status (PS) > 2, Renal failure, Neurologic abnormalities, Audiometric impairment, Hepatic, and Cardiovascular disease.

Form Completed by:	***Date:***
Treating consultant:	**Sign with Date:**

Trial Number	

"SurVIC Trial"

Informed consent

INFORMED CONSENT

I..... (Name of Patient) give my consent for participation in the study. The aims and methods of the study have been explained to me in the language understood by me. I am free to withdraw from the study at any point of time. I am given to understand that participation or withdrawal from this study would have no bearing on my treatment. The investigator has explained my rights and responsibilities to me. I have been informed that participation in this study will not change my treatment. I have informed the investigator all the treatment I have taken in the past. I agree to cooperate with the investigator and I will inform him immediately if I suffer any unusual symptom. I am also aware that the investigators may terminate my participation in the study at any time for any reason without my consent. I hereby give permission to the investigators to release the information obtained from me as result of participation in this study to regulatory authorities, government agencies, and ethics committee. I understand that they may inspect my original records. My identity will be kept confidential. I have had my questions answered to my satisfaction and have decided to be in the research study. I am aware that if I have any questions during this study, I should contact at one of the addresses listed above.

सूचित सहमति प्रपत्र

मैं..... ..... (रोगी का नाम) अध्ययन में भाग लेने के लिए मेरी सहमति दें। मेरे द्वारा समझी जाने वाली भाषा में अध्ययन के उद्देश्य और तरीके मुझे समझाए गए हैं। मैं किसी भी समय अध्ययन से हटने के लिए स्वतंत्र हूं। मुझे यह समझने के लिए दिया गया है कि इस अध्ययन में भाग लेने या वापस लेने का मेरे इलाज पर कोई असर नहीं पड़ेगा। अन्वेषक ने मुझे मेरे अधिकारों और जिम्मेदारियों के बारे में बताया है। मुझे सूचित किया गया है कि इस अध्ययन में भाग लेने से मेरे उपचार में कोई बदलाव नहीं आएगा। मैंने अन्वेषक को उन सभी उपचारों के बारे में सूचित कर दिया है जो मैंने अतीत में लिए हैं। मैं अन्वेषक के साथ सहयोग करने के लिए सहमत हूं और अगर मुझे कोई असामान्य लक्षण दिखाई देते हैं तो मैं उसे तुरंत सूचित करूंगा। मुझे यह भी पता है कि जांचकर्ता मेरी सहमति के बिना किसी भी कारण से किसी भी समय अध्ययन में मेरी भागीदारी को समाप्त कर सकते हैं। मैं जांचकर्ताओं को इस अध्ययन में मेरी भागीदारी के परिणामस्वरूप मुझसे प्राप्त जानकारी को नियामक प्राधिकरणों, सरकारी एजेंसियों और नैतिकता समिति को जारी करने की अनुमति देता हूं। मैं समझता हूँ कि वे मेरे मूल अभिलेखों का निरीक्षण कर सकते हैं। मेरी पहचान गोपनीय रखी जाएगी। मैंने अपने प्रश्नों का उत्तर अपनी संतुष्टि के अनुसार प्राप्त कर लिया है और शोध अध्ययन में शामिल होने का निर्णय लिया है। मुझे पता है कि यदि इस अध्ययन के दौरान मेरे कोई प्रश्न हैं, तो मुझे ऊपर सूचीबद्ध किसी एक पते पर संपर्क करना चाहिए।

Date/ दिनांक.....

Name of the patient:	रोगी का नाम :.....
.....	रोगी के हस्ताक्षर :.....
Signature of the patient:	अन्वेषक का नाम: .....
Name of the investigator:	अन्वेषक के हस्ताक्षर:.....
Signature of investigator:	

Counselling:

1	Patient Name	
2	Hospital CR Number	
3	Date of visit	
4	Counselling done by	
5	Result of screening	Eligible/ Ineligible
6	Patient Information Sheet hand over	Yes/No
7	Patients Queries (Enumerate)	1. 2. 3.
8	Patient Query answered	Yes/No
9	**Outcome of Counselling**	**Agree/ Disagree**
10	If disagree- mention reason	
11	Planned date of enrollment	
12	**Trial Number**	

Trial Number	

"SurVIC Trial"

Date:

Baseline:

To be filled by trial coordinator in Prescence of treating physician

Demographic Details

Date of OPD Registration		Patient Trial Number	
Name		Name of Primary Care giver with Phone Number	
Phone Number			
Date of Birth		Age/Gender	
Address 1			
House Number		Locality	
Village/Town		District	
State		Pin code	
Address 2			
House Number		Locality	
Village/Town		District	
State		Pin code	
Menopausal status	Premenopausal /postmenopausal	Marital status	
Socioeconomical status			
Education			
	Professional Degree	7	
	Graduate	6	
	Intermediate/ Diploma	5	
	High School	4	
	Middle school	3	
	Primary school	2	
	Illiterate	1	Score
Occupation			
	Professional	10	

	Semi-professional	6	
	Clerical/ Shop/ Farmer	5	
	Skilled worker	4	
	Semiskilled worker	3	
	Unskilled worker	2	
	Unemployed	1	Score:
Family Income/ Month			
	47,348 or more	12	
	23,674 – 47,347	10	
	17,756- 23,673	6	
	11,837- 17,755	4	
	7,102- 11,836	3	
	2,391- 7,101	2	
	Less than 2,390	1	Score:
			Total score:
Socioeconomic class	Modified Kupuswami score 2022		
	Upper Class	26-29	
	Upper Middle	16-25	
	Lower Middle	11-15	
	Upper lower	5-10	
	Lower	<5	

Social History – Addictions

Addictions		Type	Age of starting	Dose/ day Intensity	Dose/ Week	Duration in Years	Current status	Quit since	Category* Never/ Current/ Reformed
Smoking	Yes/ No	Cigarette/ beedi/ ……							
Non-Smoked Tobacco	Yes/ No	Paan/ Ghutkha/ Khaini							

Alcohol intake	Yes/ No	Beer/ Malt Liquor/ Wine							
Other									

Note:

***Never:** never consumed the substance;

***Current:** Consuming currently or quit for less than 3 months;

***Reformed:** Quit for 3 months or more.

Symptoms and signs

Symptoms		**Duration (days)**	**Symptoms**		**Duration (days)**
Non-Healing Ulcer	Yes/ No		Skin Fungation/ Ulcer	Yes/ No	
Pain	Yes/ No		Fatigue	Yes/ No	
Neck Swelling	Yes/ No		Denture Use	Yes/ No	
Loosening of teeth	Yes/ No		Reduced Mouth Opening	Yes/ No	
*Weight Loss	Yes/ No		Past H/o Cancer Rx	Yes/ No	
Others (please mention)					
Past H/o treatment If any-		Details			
Duration in day (Presenting symptoms to presentation -*to*- primary care/ first physician):					
Duration in day (primary physician referred -*to*- cancer Centre/ enrolling institute):					
Duration in day (Day of presentation at enrolling institute -*to*- Start of treatment):					

Note:

Weight loss: more than 10% in 6 months/ more than 5% in 3 months

Comorbidities

Charlson Comorbidity Index*			
Point score-	…….	Estimated 10-year survival	…….%
Adult Comorbidity Evaluation-27 (ACE-27)**			
Grade	……	No. of item with moderate Comorbidities	……	No. of item with severe Comorbidities…….	……

Note:

* Use https://www.mdcalc.com/calc/3917/charlson-comorbidity-index-cci

** use https://m.medicalalgorithms.com/adult-comorbidity-evaluation-27-ace-27

Family history of cancers

Cancer History in family: Yes/No;	if Yes, proceed to following section-
1st Degree/ 2nd Degree (Tick)	Tested/ Non-Tested (Tick)
Age at Malignancy:	Outcome: Alive /dead:
Type of Cancer:	Double primary: Yes/No

Nutritional History:

Diet	Veg/ Non-Veg		
Meal			
AJCC			

Physical Examination

PS(ECOG)-	0 /1/2	Height(cm)	
Weight(kg)		Weight loss (%)	
BSA (/m2)		BMI (kg/m^2)	
Muscle Wasting:	General /Temporal	Other +ve Finding:	

Clinical Examination

Primary Site:	Upper Bucco-Alveolar (BA) Complex or Lower BA complex or Tongue		
Circle the most appropriate one.	Site of tumor (Epicenter): Buccal Mucosa/ Upper GBS/ Lower GBS/ Upper Alveolus/ Lower Alveolus/ RMT/ FOM/ Oral Tongue	Right or Left	Reaching Midline: Yes/ No
		Size in cm ____x____	Proliferative/ Infiltrative/ Ulcero-infilterative
Skin Involved	Yes/ No; If yes →	Gross fungation/ Edema/ulceration (circle as applicable)	
Bone Involved	Yes/ No		
OSMF	Yes/ No	Mouth Opening in cm:	

Leukoplakia	Yes/ No	Tongue Protrusion	Restricted/ Normal
Erythroplakia	Yes/ No	c T Stage	

Neck Nodes			
Number of palpable Nodes		Level	1/2a/2b/3/4/5
Size of largest Palpable node:			
Gross ENE:	Yes/ No	What suggests ENE:	(Skin/Muscle invasion/Vessel)
Contralateral nodes (C/L)	Yes/ No	ENE in C/L Nodes	Yes/No
c N Stage		c N Stage	
Other Significant Finding			

Investigations

Biopsy

Biopsy Number		Date of Biopsy	
Histology	SCC/ Other……	Grade	1/2/3
Any special features: -	**AJCC Read**		

Laboratory Tests (on first admission for treatment)

CBC	write date of test		**LFT**	write date of test
Hb			Bilirubin(mg%) T	
RBC (10^6/ uL)			Bilirubin(mg%) D	
TLC (10^3/uL)	**Value**	**%**	Bilirubin(mg%)- I	
Neutrophil (10^3/uL)			AST/ SGOT	
Lymphocyte (10^3/uL)			ALT/ SGPT	
Monocyte (10^3/uL)			SAP	
Eosinophil (10^3/uL)			Total Protein	
Basophil (10^3/uL)			Albumin	

Large Immature Cells (LIC) (10^3/uL)			A/G Ratio	
Platelet (10^3/uL))			**HbA1c**	
COVID vaccine	Yes/ No	COVAXIN/COVISHEILD	COVID in past	Yes/No
RFT	write date of test		**Creatinine**	
Cr Clearance			**Urea**	
Viral Markers			Ejection fraction	
HBsAg/ HCV/HIV			ECG	

Radiology

Radiology			
Date:			
Staging Local Imaging	Subsite: Upper BA Complex or Lower BA complex or Tongue		
USG/ CT/MRI/PET (circle what is being done with date)	Site (Epicenter of tumor): Buccal Mucosa/ Upper GBS/ Lower GBS/ Upper Alveolus/ Lower Alveolus/ Central Alveolus/ RMT/ FOM/ Oral Tongue		
ITF	High/ Low/ Free	Supra-notch/ Infra-notch	
Size (mm)	____x_____x_____mm	DOI (mm)	
Across midline	Yes/ No		
Bone Invasion	Yes/ No	Maxilla/ Mandible	
PNI	Yes/ No		
Neck	Single/ Multiple	Level	1/2a/2b/3/4/5
Number of suspicious nodes		SAD of largest Suspicious nodes (mm)	
USG correlation		FNAC required	Yes/ No
Radiological ENE	Yes/ No	What suggests ENE	Skin/ Muscle/ Vessel
Metastatic work up	CT Thorax/ CXR/ PET CT	Date	
Findings			

Note:

* Cross section imaging in the form of CECT or MRI of the face will be done or reviewed at the accrual centers. Nodal staging will be done using standard criteria of size, shape, central fatty hilum, relation with surrounding structures by radiologist. FNAC of the equivocal nodes will be done to establish the N Status. USG neck alone would suffice to label N stage if clinician and radiologists are in Consensus.

Response rate; Treatment compliance; treatment related toxicity, postoperative complications and Quality of life.

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UICC staging 8th Edition Clinical & Pathological

Class	Description
Tx	Primary tumour cannot be assessed
T0	No evidence of primary tumour
Tis	Carcinoma in situ
T1	Tumour 2 cm or less in greatest dimension and 5 mm or less depth of invasion
T2	Tumour 2 cm or less in greatest dimension and more than 5 mm but no more than 10 mm depth of invasion or Tumour more than 2 cm but not more than 4 cm in greatest dimension and depth of invasion no more than 10 mm
T3	Tumour more than 4 cm in greatest dimension or more than 10 mm depth of invasion
T4a	Lip) Tumour invades through cortical bone, inferior alveolar nerve, floor of mouth, or skin (of the chin or the nose) (Oral cavity) Tumour invades through the cortical bone of the mandible or maxillary sinus, or invades the skin of the face
T4b	(Lip and oral cavity) Tumour invades masticator space, pterygoid plates, or skull base, or encases internal carotid artery
Nx	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1 pN1	Metastasis in a single ipsilateral lymph node, 3 cm or less in greatest dimension without extranodal extension Metastasis in a single ipsilateral lymph node, 3 cm or less in greatest dimension without extranodal extension
N2a pN2a	Metastasis in a single ipsilateral lymph node, more than 3 cm but not more than 6 cm in greatest dimension without extranodal extension Metastasis in a single ipsilateral lymph node, less than 3 cm in greatest dimension with extranodal extension or, more than 3 cm but not more than 6 cm in greatest dimension without extranodal extension
N2b pN2b	Metastasis in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension, without extranodal extension Metastasis in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension, without extranodal extension
N2c pN2c	Metastasis in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension, without extranodal extension Metastasis in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension, without extranodal extension
N3a pN3a	Metastasis in a lymph node more than 6 cm in greatest dimension without extranodal extension Metastasis in a lymph node more than 6 cm in greatest dimension without extranodal extension
N3b pN3b	Metastasis in a single or multiple lymph nodes with clinical extranodal extension Metastasis in a lymph node more than 3 cm in greatest dimension with extranodal extension or, multiple ipsilateral, or any contralateral or bilateral node(s) with extranodal extension
M0	No Distant metastasis
M1	Distant metastasis

Footnotes:

- Superficial erosion alone of bone/tooth socket by gingival primary is not sufficient to classify a tumour as T4a.
- The presence of skin involvement or soft tissue invasion with deep fixation/tethering to underlying muscle or adjacent structures or clinical signs of nerve involvement is classified as clinical extranodal extension.
- Midline nodes are considered ipsilateral nodes.
- Histological examination of a selective neck dissection specimen will ordinarily include 10 or more lymph nodes.
- Histological examination of a radical or modified radical neck dissection specimen will ordinarily include 15 or more lymph nodes.

Stage 1	T1 N0 M0		
Stage II	T2 N0 M0		
Stage III	T3 N0 M0	T1-T3 N1 M0	
Stage IVA	T4a N0 M0	T4a N1 Mo	T1-T4a N2 M0
Stage IVB	T4b any N M0	Any T N3 M0	
Stage IVC	Any T any N M1		

Ref: TNM classification of Malignant tumors 'UICC 8th Edition'

Trial Number	

"SurVIC Trial"

Restaging: "Applicable only for ICT arm"

Method of restaging:
Clinical Examination (CE) only/ or CT Scan/ or MRI/ or PET CT

Response on clinical assessment	
*Progressive disease/ Stable disease/ Complete Response/ Partial Response	

***Note: as per chaukar et al**

Complete response: No evidence of clinical disease.
Partial response: 50% decrease in the size of the lesion (either primary or nodes)
Stable < 50% decrease in the size of the lesion (Either primary or nodes)
Progressive disease - >25% increase in the lesion or appearance of new lesions (Either primary vs Nodes)

			Radiology
Date:			
Re-Staging Local Imaging	Subsite: Upper BA Complex or Lower BA complex or Tongue		
USG/ CT/MRI/PET (circle what is being done with date)	Site (Epicenter of tumor): Buccal Mucosa/ Upper GBS/ Lower GBS/ Upper Alveolus/ Lower Alveolus/ Central Alveolus/ RMT/ FOM/ Oral Tongue		
ITF	High/ Low/ Free	Supra-notch/ Infra-notch	
Size (mm)	____x_____x_____mm	DOI (mm)	
Across midline	Yes/ No		
Bone Invasion	Yes/ No	Maxilla/ Mandible	
PNI	Yes/ No		
Neck	Single/ Multiple	Level	1/2a/2b/3/4/5
Number of suspicious nodes		SAD of largest Suspicious nodes (mm)	
USG correlation		FNAC required	Yes/ No
Radiological ENE	Yes/ No	What suggests ENE	Skin/ Muscle/ Vessel
Response category	CR/ PR/ SD/ PD		

*RECIST v1.1 Criteria

Complete response (CR): Disappearance of all target and non-target lesions SAD of previously pathological lymph nodes should be <10 mm
Partial response (PR): ≥30% decrease in the SLD of target lesions.
Stable disease (SD): neither unequivocal progression or regression.
Progressive disease (PD): ≥20% increase in the SLD of target lesions compared to smallest SLD in the study (nadir) AND ≥5 mm SLD increase OR progression of non-target lesions OR new lesions.

Online calculator Ref: https://radcalculators.org/recist-1-1-calculator/

Article Ref: Eisenhauer EA, Therasse P, Bogaerts J, Schwartz LH, Sargent D, Ford R, Dancey J, Arbuck S, Gwyther S, Mooney M, Rubinstein L, Shankar L, Dodd L, Kaplan R, Lacombe D, Verweij J. New response evaluation criteria in solid tumours: revised RECIST guideline (version 1.1). Eur J Cancer. 2009 Jan;45(2):228-47

Trial Number	

"SurVIC Trial"

Quality of Life assessment: FACT G/ H&N/ COST/ Fatigue score

Please Score each question with your response (as mentioned below), as it applies to the past 7 days.

0	1	2	3	4
बिल्कुल नहीं Not at all	थोड़ा सा A little bit	कुछ कुछ some what	काफ़ी कुछ Quite a bit.	बहुत अधिक very Much

	Scale: Domain	Score 0/1/2/3/4
FACT: Physical well-being: शारीरिक स्वस्थता (PWB)		
GP1	I have a lack of energy. मुझमें ताकत की कमी है	
GP2	I have nausea. मुझे उबकाई आती है	
GP3	Because of my physical condition, I have trouble meeting the needs of my family. मेरी शारीरिक हालत के कारण मुझे अपने परिवार की ज़रूरतें पूरी करने में कठिनाई होती है	
GP4	I have pain. मुझे दर्द रहता है	
GP5	I am bothered by side effects of treatment. इलाज के बुरे प्रभाव से मुझे परेशानी होती है	
GP6	I feel ill. मैं बीमार महसूस करता/करती हूँ	
GP7	I am forced to spend time in bed. मुझे बिस्तर में पड़े रहना पड़ता है	
SOCIAL/FAMILY WELL-BEING: सामाजिक / पारिवारिक सुख (SWB)		
GS1	I feel close to my friends. मैं अपने दोस्तों को करीब महसूस करता/करती हूँ	
GS2	I get emotional support from my family. अपने परिवार से मुझे भावनात्मक सहारा मिलता है	
GS3	I get support from my friends. मुझे अपने दोस्तों से सहारा मिलता है	
GS4	My family has accepted my illness. मेरे परिवार ने मेरी बीमारी स्वीकार कर ली है	
GS5	I am satisfied with family communication about my illness. मेरी बीमारी के बारे में परिवार में जो बातचीत होती है, उससे मैं संतुष्ट हूँ	
GS6	I feel close to my partner (or the person who is my main support). मैं अपने साथी (या मुख्य मददगार) को करीब महसूस करता/करती हूँ	
GS7	*Regardless of your current level of sexual activity, please answer the following question. If you prefer not to answer it, please move to the next section. वर्तमान में आपके शारीरिक संबंध कैसे हैं इस पर ध्यान दिए बिना, कृपया निम्नलिखित प्रश्न का उत्तर दें। यदि आप इस प्रश्न का उत्तर देना नहीं चाहें, तो कृपया इस बॉक्स पर निशान लगाएं और अगले खंड में जाएं।* I am satisfied with my sex life. मैं अपने यौन जीवन से संतुष्ट हूँ	
EMOTIONAL WELL-BEING: भावनात्मक स्वस्थता (EWB)		
GE1	I feel said. मैं उदास रहता/रहती हूँ	
GE2	I am satisfied with how I am copying with my illness. मैं अपनी बीमारी का जिस तरह सामना कर रहा/रही हूँ उससे संतुष्ट हूँ	
GE3	I am losing hope in the fight against my illness. अपनी बीमारी से लड़ते हुए मैं आशा खो रहा/रही हूँ	
GE4	I feel nervous. मुझे घबराहट होती है	
GE5	I worry about dying. मैं मृत्यु के बारे में चिंतित हूँ	
GE6	I worry that my condition will get worse. मैं चिंतित हूँ कि कहीं मेरी हालत और न बिगड़ जाए	

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FUNCTIONAL WELL-BEING: कार्यात्मक स्वस्थता (FWB)		
GF1	I am able to work including work at home. मैं काम (घर के कामों सहित) करने लायक हूँ	
GF2	My work is (including work at home) fulfilling. मेरा काम (घर के कामों सहित) मेरे अनुकूल है	
GF3	I am able to enjoy life. मैं जीवन का आनंद लेता/लेती हूँ	
GF4	I have accepted my illness. मैंने अपनी बीमारी को स्वीकार कर लिया है	
GF5	I am sleeping well. मुझे अच्छी नींद आती है	
GF6	I am enjoying the things I usually do for fun. मैं मज़े के लिए जो करता/करती हूँ, उससे मुझे खुशी होती है	
GF7	I am content with the quality of my life right now. अपने वर्तमान जीवन-स्तर से मैं संतुष्ट हूँ	
Head and Neck v4-0		
HN1	I am able to eat the foods that I like. मैं अपनी पसंद का भोजन खा सकता/सकती हूँ	
HN2	My mouth is dry. मेरा मुँह सूखा हुआ है	
HN3	I have trouble breathing. मुझे साँस लेने में परेशानी होती है	
HN4	My voice has its usual quality and strength. मेरी आवाज़ में सामान्य रूप की गुणवत्ता और ताकत है	
HN5	I am able to east as much food as I want. मैं जितना चाहूँ उतना भोजन खा सकता/सकती हूँ	
HN6	I am unhappy with how my face and neck look. मेरा चेहरा और गर्दन जैसे दिखते हैं मैं उससे नाखुश हूँ	
HN7	I can swallow naturally and easily मैं स्वाभाविक रूप से और आसानी से निगल सकता/सकती हूँ	
HN8	I smoke/ consume tobacco products मैं सिगरेट या अन्य तंबाकू आधारित चीज़ें पीता/पीती हूँ	
HN9	I drink alcohol. मैं शराब पीता/पीती हूँ	
HN10	I am able to communicate with others. मैं दूसरों को अपने विचार और अपनी भावनाएँ व्यक्त कर सकता/सकती हूँ	
HN11	I can eat solid foods. मैं ठोस भोजन खा सकता/सकती हूँ	
HN12	I have pain in my mouth throat or neck. मेरे मुँह, गले या गर्दन में दर्द होता है	
Fatigue v2.0		
HI7	I feel fatigued. मैं पस्त रहता/रहती हूँ	
HI12	I feel weak all over. मुझे पूरे शरीर में कमज़ोरी महसूस होती है	
An1	I feel listless (washed out). मैं बेजान महसूस करता/करती हूँ	
An2	I feel tired. मुझे थकान महसूस होती है	
An3	I have trouble starting things because I am tired. थकान की वजह से मुझे कोई भी काम शुरू करने में परेशानी होती है	
An4	I have trouble finishing things because I am tired. थकान की वजह से मुझे कोई भी काम पूरा करने में परेशानी होती है	
An5	I have energy. मैं चुस्त रहता/रहती हूँ	
An7	I am able to do my usual activities. मैं अपने रोज़मर्रा के कामकाज कर पाता/पाती हूँ	
An8	I need to sleep during the day. मुझे दिन में सोने की ज़रूरत पड़ती है	
An12	I am too tired to eat. थकान की वजह से मुझसे खाया नहीं जाता	

An14	I need help doing my usual activities. अपने रोज़मर्रा के कामकाज करने में मुझे मदद की ज़रूरत पड़ती है	
An15	I am frustrated by being too tired to do the things I want to do. मैं निराश हूँ क्योंकि ज़्यादा थकान होने से मैं वे चीज़ें नहीं कर पाता/पाती जो मैं करना चाहता/चाहती हूँ	
An15	I have to limit my social activity because I am tired. थकान के कारण मुझे अपनी सामाजिक गतिविधियाँ सीमित करनी पड़ती हैं	
COST FACIT v2.0		
FT1	I know that I have enough money in savings, retirement, or assets to cover the costs of my treatment. मुझे पता है कि मेरे पास अपने इलाज के खर्च को पूरा करने के लिए बचत, सेवानिवृत्ति, या संपत्ति में पर्याप्त पैसा है	
FT2	My out-of-pocket medical expenses are more than I thought they would be. मेरे इलाज के लिए मेरी जेब से होने वाला खर्च, जितना मैंने सोचा था उससे अधिक है	
FT3	I worry about the financial problems I will have in the future as a result of my illness or treatment. अपनी बीमारी या इलाज के कारण भविष्य में मुझे होने वाली आर्थिक समस्याओं के बारे में चिंता होती है	
FT4	I feel I have no choice about the amount of money I spend on care. मुझे लगता है कि मेरे पास देखभाल पर खर्च होने वाली राशि के बारे में कोई विकल्प नहीं है	
FT5	I am frustrated that I cannot work or contribute as much as I usually do. मैं निराश हूँ कि मैं उतना काम या योगदान नहीं कर पा रहा जितना मैं आमतौर पर करता हूँ	
FT6	I am satisfied with my current financial situation. अपनी वर्तमान आर्थिक स्थिति से मैं संतुष्ट हूँ	
FT7	I am able to meet my monthly expenses. मैं अपने मासिक खर्चों को पूरा कर सकता/ सकती हूँ	
FT8	I feel financially stressed. मुझे लगता है कि मुझे आर्थिक समस्याएँ है	
FT9	I am concerned about keeping my job and income, including paid work at home. मैं अपनी नौकरी और आय रखने के लिए चिंतित हूँ, जिसमें घर पर वैतनिक काम भी शामिल है	
FT10	My cancer or treatment has reduced my satisfaction with my present financial situation. मेरे कैंसर या उपचार ने मेरी वर्तमान आर्थिक स्थिति के साथ मेरी संतुष्टि को कम कर दिया है	
FT11	I feel in control of my financial situation. मैं अपनी आर्थिक स्थिति पर नियंत्रण महसूस करता हूँ	
FT12	My illness has been a financial hardship to my family and me. मेरी बीमारी मेरे परिवार और मेरे लिए एक आर्थिक कठिनाई रही है	

Timing	**SURG Arm**	**ICT Arm**
B	**At start of treatment**	**At start of treatment**
PS	**After Surgery at 4 weeks**	**After surgery at 4 weeks**
F-0	**After Radiotherapy at 4 weeks**	**After Radiotherapy at 4 weeks**
F-3	**3-month post treatment**	**3- months post treatment**
F-6	**6m**	
F-9	**9m**	
F-12	**12m**	

F-18	**18m**	
F-24	**24m**	
F-30	**30m**	
F-36	**36m**	

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SURGICAL TREATMENT

Date of Surgery	
Resection of Primary	Wide excision of soft tissue with
Bone Resection (circle as appropriate): Nil Segmental Mandibulectomy Marginal mandibulectomy Upper Alveolectomy Infrastructure Maxillectomy Central arch resection Zygoma resection	ITF Clearance (circle as appropriate): Nil Standard infratemporal Fossa Clearance High infratemporal Fossa Clearance
Lymphadenectomy	
Ipsilateral only/ Bilateral	
Level 1-3/ Level 1-4/ Level 1-5	
Sternocleidomastoid Muscle- Preserved/ Sacrificed	
Internal Jugular Vein- Preserved/ Sacrificed	
Spinal Accessory Nerve- Preserved/ Sacrificed	
Reconstruction-	
Primary Closure/ PMMC/ DP Flap/ Submental/ Nasolabial/ Skip Graft/ Buccal Fat pad/ Free radial/ Free Anterolateral Thigh Flap / Free Fibular Flap/ Other_____	
Tracheostomy	
Yes/No, if Yes Reason_____ Removed on Day_____	
Feeding Management	
Ryle's Tube, kept till which post operative day_____ Feeding Jejunostomy/ Per Cutaneous Gastrostomy- if yes Reason_____	
Surgical Duration in Minutes	
Duration of Primary resection: Duration of neck Dissection: Duration of Reconstruction: Total surgical Duration:	
Intraoperative Complications (if any name it)	

Blood Loss (ml)			
Intra operative Blood Transfusions	Yes/ No	**Number of units transfused**	
Postoperative transfusions	Yes/ No	**Number of units transfused**	
ICU Stay	Yes/ No	**ICU days**	
Revision surgery (Y/N) (procedure)			
Duration of hospitalization (days)			
Parenteral antibiotics use (days)			
Condition on discharge		Drain out/insitu; TT out/ insitu; FT out/ Insitu	
Oral antibiotics use (days)			
Readmission			

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Postoperative Complication (up to 30d)

Post operative complications	Yes/ No
Grade of complications*	I/ II/ IIIa/ IIIb/ IVa/ IVb/ V
Postoperative day of recording complication	

Types	Details of treatment
Local wound Infection	
Superficial wound infection/ Deep would infection	
Systemic infection	
Chest infection/ Sepsis/ Septicemia/ UTI/ _____	
Flap related	
Wound dehiscence/ partial flap loss / Total flap loss	
Other wound related	
Hemorrhage/ Chyle leak/ OC fistula/ Salivary fistula	
GI- HPB	
Gastro-paresis/ Delayed gastric emptying/ Aspiration / Deranged liver functions / Liver Failure	
Pulmonary	
DVT/ Pleural effusion/ Embolism/ Respiratory Failure/_____	
Renal	
Electrolyte imbalance/ Deranged renal function/ Renal Failure	
Cardiovascular	
Hypotension/ Cardiac failure/ Hemorrhagic shock / _____	
Other systemic	
Anemia/ Fever of unknown origin/ _____	

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Serious adverse event (SAE)

SAE is any untoward medical occurrence that at any dose that results in

1. Death,
2. life-threatening (i.e., the subject is at risk of death at the time of the event),
3. requires inpatient hospitalization or prolongation of existing hospitalization,
4. Results in persistent or significant disability or incapacity,
5. Other important medical events which, in the opinion of the investigator, are likely to become serious if untreated, or as defined in the protocol
6. Significant overdose: In case of a significant overdose of a study drug, this has to be reported as a serious adverse event.

Clavien Dindo classification

Grades	Definition
Grade I:	Any deviation from the normal postoperative course without the need for pharmacological treatment or surgical, endoscopic and radiological interventions. Acceptable therapeutic regimens are: drugs as antiemetics, antipyretics, analgetics, diuretics and electrolytes and physiotherapy. This grade also includes wound infections opened at the bedside.
Grade II:	Requiring pharmacological treatment with drugs other than such allowed for grade I complications. Blood transfusions and total parenteral nutrition are also included.
Grade III:	Requiring surgical, endoscopic or radiological intervention
Grade III-a:	intervention not under general anesthesia
Grade III-b:	intervention under general anesthesia
Grade IV:	Life-threatening complication (including CNS complications)‡ requiring IC/ICU-management
Grade IV-a:	single organ dysfunction (including dialysis)
Grade IV-b:	multi organ dysfunction
Grade V:	Death of a patient

Ref: Clavien PA, Barkun J, De Oliveira ML, Vauthey JN, Dindo D, Schulick RD, De Santibañes E, Pekolj J, Slankamenac K, Bassi C, Graf R. The Clavien-Dindo classification of surgical complications: five-year experience. Annals of surgery. 2009 Aug 1;250(2):187-96.

Histopathology

Site of Tumor		**Date of reporting**	

Upper Lip/ Lower Lip/ Lateral Tongue/ Ventral Tongue/ Dorsal Tongue/ Anterior two third tongue/ Upper Gingiva/ Lower Gingiva/ Anterior Floor of mouth/ Floor of mouth/ Hard palate/ Buccal mucosa/ Vestibule- upper/ Vestibule- Lower/ Alveolar process- upper/ Alveolar process- Lower/ Retromolar trigone			
Tumor Laterality	Right/ Left/ Midline/ Unspecified		
Tumor focality	Unifocal/ Multifocal/ Can't determined		
Tumor size-	____x_____x_____	Greatest tumor dimension	**_____mm**
Depth of Invasion-	**_____mm**	Tumor thickness-	**_____mm**
Histological Type			
Squamous cell carcinoma/ conventional Acantholytic squamous cell carcinoma/ Adenosquamous carcinoma/ Basaloid squamous cell carcinoma/ Carcinoma cuniculatum/ Papillary squamous cell carcinoma/ Spindle cell squamous cell carcinoma/ Verrucous squamous cell carcinoma/ Lymphoepithelial carcinoma			
Histological Grade	G1/ G2/G3/Gx		
Tumor extensions	Skin/ bone/ Nerve/ other		
Specimen Margin	Involved/ Close/ Free-		
Closest Margin Distance/ margin orientation-			
Lymho Vascular emboli			
Not Identified/ Present/Micro/ Major			
Perineural invasion			
Not Identified/ Present/ Extent of invasion-			
Worst Pattern of Invasion			
WPOI 5/ WPOI 1-4			
Residual tumor assessment	**RX/R0/R1/R2**	**Major salivary gland**	**involved/ free**
Regional Nodes			
Nodes- submitted/ Not Submitted			
Nodes submitted Oriented or unoriented			
Total Number of Nodes Identified-			
Number of Nodes are Involved-			
Laterality of Involved nodes- Ipsilateral/ Contralateral/ Bilateral			
Size of largest metastatic deposit (cm)-			
Level 1a (Total Nodes/ Positive Nodes/size of Deposit)			
Level 1b(Total Nodes/ Positive Nodes/size of Deposit)			

Level 2a (Total Nodes/ Positive Nodes/size of Deposit)			
Level 2b (Total Nodes/ Positive Nodes/size of Deposit)			
Level 3 (Total Nodes/ Positive Nodes/size of Deposit)			
Level 4 (Total Nodes/ Positive Nodes/size of Deposit)			
Level 5 (Total Nodes/ Positive Nodes/size of Deposit)			
Extra nodal Extension (ENE)		**Y/N**	
Distance from Lymph node capsule (mm)-			
ENEma (>2 mm)			
ENEmi (≤2 mm)			
pT		**pN**	

Treatment plan after HPE

Follow up/ Adjuvant Radiotherapy alone/ Adjuvant CCRT

post-surgical days

"SurVIC Trial"

Planned Treatment details-

Plan as per HPE			
Radiotherapy			
Dose of radiation planned (Total dose)	Field	Number of fractions	
Dose per fraction		RT Technique	2D/ 3D CRT/ IMRT-VMAT (SIB)/ IMRT-VMAT (Sequential)
Date of RT start		Date of RT completion	
Concurrent treatment			
Concurrent CT required	Yes/No	Concurrent drug	Cisplatin/ Carboplatin/ Cetuximab/ Nimotuzumab/ _____
Indicated but not given (reason)	Age/ Tolerance issues/ deranged Renal function/ _____		
Cycles of chemotherapy		schedule	Weekly/ 3-weekly
		Dose of chemotherapy	
Actual treatment delivery			
Dose delivered		No of fractions	
Dose per fraction		RT Technique	2D/ 3D CRT/ IMRT-VMAT (SIB)/ IMRT-VMAT (Sequential)
Date of RT start		Date of RT completion	
Adaptive planning (re-plan) needed	Yes/No	Reason for re-plan	
Treatment break	Yes/ No	How many days break	
Reason for break	Grade > III toxicity/ Defaulted/ logistics/ _____		
Gap correction of any			
Concurrent CT (Y/N)			
Cisplatin/ Carbo/ Nimotuzumab/other…..			
Dose of chemo		Cycles of chemotherapy	
Dose of chemotherapy			
Dose modification	Yes/ No	Reason for dose modification	

Trial Number	

"SurVIC Trial"

Toxicity during Radiotherapy (RTOG Toxicity Assessment)
(Write appropriate Grade)

Treatment week	Skin	Mucosa	Pharynx	Larynx	Salivary Gland	Weight	CBC
Week 1							
Week 2							
Week 3							
Week 4							
Week 4							
Week 5							
Week 6							
Week 7							
Week 8							

Trial Number	

"SurVIC Trial"

Chemotherapy
Treatment Protocol
DCF Template

NAME_____AGE_____SEX_____HOSPITAL NO_____
BSA_____REGIMEN: DCF
*Weight monitoring before each cycle and D8 followup for neutropenia

DATE	...../..../....	...../..../....	...../..../....
CYCLE NO/DAY			
Weight			
Cap Apprepetant 125 mg d1/80 mg day 2 and 3			
PREMEDICATIONS :Inj Dexamethasone 12mg+ chlorpheniramine(piritone)10mg+Ondansetron 8mg + Rantac 50mg in 100ml NS give 30mins before chemo D 1-5			
Inj.DOCETAXEL 75 mg/m2 in 500 ml NS over 1 hour day 1only			
Inj NS 500 ml with 10 miliequilant KCL IV over 60 mins day 1 only			
Inj Mannitol 200ML IV over 15 -20 mins day 1 only			
Cisplatin 75 mg/m ^{2} V in 1000 ml NS over 1 hours on D1 only (start after completion of docetaxel)			
Inj NS 500 ml with 10 miliequilant KCL IV over 60 mins day 1 only			
5FU 750 mg/m2 IV THROUGH INFUSION PUMP over 24 hours D 1-5			

Date of start of chemotherapy
Regimen: DCF/ DCX/ CF/ .....

	Cycle 1	Cycle 2	Cycle 3
Date of start			
ECOG PS			
Lab Values			
Hb			
ANC			
Platelet			
Bilirubin			
SGOT/SGPT			
Creatinine			
Cr Clearance			

Blood Sugar			
Other details			
Primary/ Secondary GCSF			
Dose delay			
Reason for delay			
Number of days delayed			
Dose modification			
Reason for dose modification			

Note

Haematological: Haemoglobin > 9gm/dl, ANC ≥ 1500/cmm3, Platelet ≥100000/cmm3
Liver Function test: Bilirubin ≤2 x upper limit normal (ULN), AST/ALT/ ALP ≤ 2.5 x ULN
Renal Function test: Creatinine ≤ 1.5 ULN, Creatinine Clearance ≥60 ml/min.

Trial Number	

"SurVIC Trial"

Concomitant medicines

S. No.	Drug name	Dose	Frequency	Date of start	Date of stop	Remarks

Adverse Event
Please grade according to CTCAE

AE ID#	AE	**Cycle 1**	**Cycle 2**	**Cycle 3**
A	Thrombocytopenia			
B	Neutropenia			
C	Febrile Neutropenia			
D	Hyponatremia			
E	Hypokalemia			
F	Hyperbilirubinemia			
G	Anemia			
H	Transaminitis			
I	Mucositis			
J	Vomiting			
K	Diarrhea			
L	Constipation			
M	Skin rashes			

N	Hand Foot Syndrome			
O	Fatigue			
P	Cardiotoxicity			
Q	Neurotoxicity			

"SurVIC Trial"

Adverse Events management

	Description on management			
Chemotherapy cycle:				
AE →				
Start Date				
End Date				
Admission required				
Duration of admission				
Antibiotics given				
Number of days of antibiotics				
Nadir ANC				
Nadir Platelets				
Focus of infection				
Transfusion				
GCSF given				
Dose reduction planned from next cycle				
Other management				
Drug 1				
Drug 2				
Drug 3				

Please see the Adverse event monitoring chart- eg Alphabet with cycle number (A1- means Thrombocytopenia cycle 1)

Trial Number	

"SurVIC Trial"

Protocol deviation due to chemotherapy

#	Start date	End date	Description	Category (Circle as applicable)	Does deviation/ unanticipated problem have the potential to*:			Reported to IRB	PI sign date
					Impact subject safety	Affect data integrity	Affect subject's willingness to participate?		
				Consent Deviation Drug Administration/Accountability Enrollment Deviation Procedural Deviation Loss of Confidentiality Other (describe)				Date of reporting Or Not applicable	
				Consent Deviation Drug Administration/Accountability Enrollment Deviation Procedural Deviation Loss of Confidentiality Other (describe)				Date of reporting Or Not applicable	
				Consent Deviation Drug Administration/Accountability Enrollment Deviation Procedural Deviation Loss of Confidentiality Other (describe)				Date of reporting Or Not applicable	
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				Consent Deviation Drug Administration/Accountability Enrollment Deviation Procedural Deviation Loss of Confidentiality Other (describe)				Date of reporting Or Not applicable	
				Consent Deviation Drug Administration/Accountability Enrollment Deviation Procedural Deviation Loss of Confidentiality Other (describe)				Date of reporting Or Not applicable	
				Consent Deviation Drug Administration/Accountability Enrollment Deviation Procedural Deviation Loss of Confidentiality Other (describe)				Date of reporting Or Not applicable	
				Consent Deviation Drug Administration/Accountability Enrollment Deviation Procedural Deviation Loss of Confidentiality Other (describe)				Date of reporting Or Not applicable	
				Consent Deviation Drug Administration/Accountability Enrollment Deviation Procedural Deviation Loss of Confidentiality Other (describe)				Date of reporting Or Not applicable	
				Consent Deviation Drug Administration/Accountability Enrollment Deviation Procedural Deviation Loss of Confidentiality Other (describe)				Date of reporting Or Not applicable	
				Consent Deviation Drug Administration/Accountability Enrollment Deviation Procedural Deviation Loss of Confidentiality Other (describe)				Date of reporting Or Not applicable	

*If one or more is answered yes for any event, it must be reported to the IRB promptly (14 business days from notification of or becoming aware of the event).

Trial Number	

"SurVIC Trial"

Follow up details

Telephone contact

If Telephone contact not performed, complete the Subject Deviation form

	Date of contact attempt	Time	Contact occurred	Outcome
Attempt 1			Yes /No	No answer Answered
Attempt 2				
Attempt 3				

Date of telephone contact completed:

QUESTION(S) TO BE ASKED	FORM No	
Since your last study contact, have you had any changes in health status, medical conditions, or adverse events?		Yes/ No
Concomitant Medications Log completed *(if applicable)*?		
Adverse Event Symptoms reviewed with Subject?		
Adverse Event Tracking Log Completed (same log form for all visits)?		
If any AE has 'Yes' in Serious column, complete SAE form and enter the information in Subject Console > SAEs screen of OnCore?		
Does the medical history form need to be updated?		
Were there any activities that deviated from the defined protocol?		
If yes, completed the Deviation/Violation form and enter the information in the Subject Console > Deviation's screen of On Core?		
Subject payment confirmed (if applicable)		
OTHER QUESTION TO ASK(if applicable)		

COMMENTS:
TELEPHONE CONTACT CONDUCTED BY:
FORM COMPLETED BY: **DATE:**

Trial Number	

"SurVIC Trial"

Follow up report

Clinical and Radiological Follow up Assessment Report:

Date of follow up assessment

Follow up No.	
Clinical Examination	
Clinical Examination Date	
Clinical Examination findings	
Imaging	
Date of Imaging	
Imaging type: USG/ CT/ MRI/ PET CT	
Imaging findings	
Biopsy	
Biopsy date	
Biopsy report	
Final Status	
Follow up status Date	
Follow up Status: Disease free / recurrence	
Site: Local/ Loco-regional/ LR+Distant/ Distant only	
Alive/ Death	
If dead, cause of death	
Date of death	
Place of death (Hospital/ Home)	

Trial Number	

"SurVIC Trial"

Patient removal From Study

Name:			
Hospital Number		Trial Number	
Evaluation done by (Doctor)			
Who was present during evaluation			
Reason for removal from clinical trial (tick all that applies)		1. Completed protocol treatment and follow up 2. Patient wishes to withdraw 3. Withdrawn due to toxicity 4. Withdrawn due to alternate treatment plan 5. Withdrawn due to lack of benefit from trial medicine 6. Other reasons: _____ _____ _____ _____	
Time spent in counselling (minutes)		Location where counselling done	
Alternate treatment options explained details			
Patient asked for queries YES/ NO			
Specific queries, if any			
EDC entries (date of completion)			
IEC intimation, if applicable			
Next Treatment Plan:			
Next follow up visit planned on:			
Other remarks			

Name of doctor
Sign/ Date

Name of coordinator
Sign/ Date