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USE OF LIQUID BIOPSY TO TAILOR THE NEOADJUVANT TREATMENT IN LOCALLY ADVANCED RECTAL CANCERS: FINDING SOLUTION FOR AGGRESSIVE CANCERS IN LMICS

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Background: There has been a steady rise in young onset, aggressive rectal cancers especially in low middle income countries. These cancers are often refractory to traditional neo-adjuvant chemo-radiation (n-CRT) strategy. However, identification of poor responders to neoadjuvant treatment (NAT) during the treatment course remains a challenge, often leading to poor survival outcomes. This study investigates the use of liquid biopsy (cell-free or circulating DNA) to tailor NAT for locally advanced rectal cancers (LARC) by identifying poor responders early.

Materials and Methods

Study design:Single arm, Phase II prospective interventional feasibility trial

Study population: High risk LARC [cT3,T4 Node positive and either of: EMVI+ / Lateral pelvic nodes/ Involved MRF/long-segment disease(more than 5cm)]

Primary objective: To study the association of clinico-pathological features and ctDNA kinetics with the response to nCRT

Secondary objectives: (a)To study the correlation of ctDNA kinetics with survival statistics (b) To study the role of ctDNA in risk-stratification of LARC patients

Study sites: 3 tertiary cancer centres across Indian sub-continent have confirmed participation

Study period: 4 years (1 year of recruitment; 3 years of follow-up)

Sample Size 264 patients

Results: Patients with high risk LARC will be staged using MRI pelvis and computed tomography scan of thorax and abdomen. Patients will receive long-course CRT and response assessment will be done after 6 weeks. Based on clinical and radiological response, patients will be segregated into 3 categories - complete or near-complete response, partial response and stable-progressive disease. Samples of ct-DNA will be collected at baseline, after completion of CRT and at 6 weeks after CRT. Any patient with stable disease will be planned for surgery at 6-7 weeks. Patients with partial or complete response and low ctDNA will be offered consolidation chemotherapy as per the PRODIGE-23 protocol and then repeat response assessment done. Patients with complete clinical response will be offered Watch and wait policy, while others will be planned for surgery. Patients with high ctDNA at 6 weeks in presence of partial or complete response will be planned for surgery, without any consolidation chemotherapy. Interim analysis will be done at 50% patient recruitment. After approval from Data safety monitoring unit, further recruitment would be done. Stastical analysis would be done to correlate the ctDNA kinetics with clinico-pathological disease parameters with the response assessment.

Conclusions: This study aims to study the role of liquid biopsy in segregating and tailoring the treatment of high risk LARCs. This may serve as a potential non-invasive tool to identify the poor responders to CRT early and offer appropriate treatment strategy.

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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

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Background: Most oral cancer in India is present in advanced stage and tends 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. Despite an excellent response rate, attempted Neoadjuvant chemotherapy trials failed to show oncological advantage. Earlier studies suffered by their heterogenous patient population, including all head and neck subsites, and included both inoperable cancer/ early-stage operable cases. Due to such patient selection, the intended results were never met. Patients with biologically aggressive diseases are more likely to benefit. Hence we want to find out the oncological advantage of adding induction chemotherapy to oral squamous cell cancer with advanced nodal disease (N2-N3).

Materials and Methods: Primary objective: To compare the survival outcomes of adding induction chemotherapy (ICT) before surgery in patients of oral cancer with the advanced nodal disease in terms of 2 years of disease-free survival. Secondary Objectives: To assess the following outcomes between the treatment arms- 2-year–> Overall survival, clinical & Pathological Response rate, treatment compliance, and treatment completion rate, Averse events, and treatment-related toxicity using Common Terminology Criteria for Adverse Events (CTCAE v5.0), Quality of life using (FACT -G and FACT- HN) and postoperative complications using modified Clavien-Dindo classification.

Study Population: Operable Oral cavity Squamous cell carcinoma with advanced nodal disease (N2-N3).

Inclusion criteria: Biopsy-proven, operable oral Squamous cell carcinoma cT1-T4; cN2-N3, with adequate organ function, Age- 18-65 years, ECOG-PS:0-2

Design: Open-label, Multicentric, randomized controlled trial with an allocation ratio of 1:1

Setting: 6 leading cancer centers of India.

Sample size: The primary endpoint is disease-free survival. To have 80% power to detect a hazard ratio of 0.67, a total of 184 events are needed using a two-sided significance level. Assuming an accrual rate of 15 monthly patients, 300 patients need to be recruited. The DFS analysis will occur 32 months after the start of the trial. The follow-up of patients will continue for five years. The analysis of OS will be conducted when 184 deaths are observed.

Results: Treatment arms: Standard Arm (SURG arm): Surgery followed by adjuvant Radiotherapy ± Concurrent Chemotherapy Experimental Arm (ICT): 2# TPF-based induction chemotherapy then Surgery followed by adjuvant Radiotherapy ± Concurrent Chemotherapy

Primary Endpoints: Primary- Disease-free survival

Conclusions: The current trial should either establish the superiority of ICT or put a complete pause on futile efforts of ICT in OSCC with advanced nodal disease. It can be practice-changing data for Indian patients.

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FEASIBILITY OF BRCA1 AND BRCA2 TESTING AMONG NIGERIAN WOMEN WITH BREAST CANCER

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Background: Breast cancer is the most common malignancy in Nigerian females. Among Nigerian women, breast cancer is diagnosed at a younger age and later stage. A higher proportion of patients have tumors that are triple negative and both overall and stage-specific survival are lower compared to North American or European populations. The prevalence of *BRCA1* and *BRCA2* mutations in Nigeria are exceptionally high, with rates of 7.0% and 4.1% respectively. The American Society of Breast Surgeons recommends that genetic testing become the standard of care for all breast cancer patients. However, in Nigeria, the understanding of hereditary breast cancer gene variant prevalence, penetrance, and relative risk of associated cancers is limited. Furthermore, the National Comprehensive Cancer Network Guidelines for Sub-Saharan Africa state that genetic testing is costly and technically challenging.

Our preliminary data suggests that lack of genetic counseling services, pathways for referral, and testing facilities impede the implementation of genetic testing in clinical practice. Despite barriers to access, there is interest in expanding care to include genetic testing and improve understanding of familial risk. The objective of this study is to assess the feasibility of *BRCA1/2* testing among Nigerian women with breast cancer. This work lays the foundation for introducing breast cancer genetic testing as the standard of care in Nigeria. Potential clinical impacts include risk stratification and assessment of *BRCA1/2* carriers, personalized breast cancer management, and cascaded family screening.

Materials and Methods: This observational study aims to enroll 100 patients with invasive breast cancer from three teaching hospitals in Nigeria over six months. Participant saliva samples will be collected at enrollment and shipped for remote testing. Participants will subsequently receive interpretation of their results, genetic counseling, and clinical follow-up to explore risk reduction options.

This study will assess the feasibility of saliva-based *BRCA1/2* remote genetic testing and offer clinical feedback to breast cancer patients in Nigeria. Secondary endpoints include determining the prevalence of *BRCA1/2* mutations in this population, clinical evaluation of treatment-related events, and patient-reported outcomes and experience through qualitative surveys.

Results: n/a

Conclusions

Feasibility: This pilot study is funded by the Health Equity Grand Challenge at the University Health Network, Toronto, Canada. Future directions may include a larger-scale multi-country study with expansion to other West African countries. Research Ethics Board approval is underway, and recruitment will commence in October 2023.