

## ESTRO 2024

### Highlights: Two Clinical Trials on Cancer Treatment using modern radiotherapy

**This review summarizes two clinical trials focusing on different cancer treatment modalities: the STORM trial for oligorecurrent prostate cancer (PCa) with lymph node metastases in the pelvis after primary treatment, and the ORATOR trial comparing radiation therapy (RT) versus transoral robotic surgery (TORS) for early-stage oropharyngeal cancer.**

The STORM trial (1), an international phase II, open-label, randomized superiority trial, addressed the management of pelvic nodal recurrences in prostate PCa patients. The trial evaluated metastasis-directed therapy (MDT) using stereotactic radiotherapy (SBRT) versus elective nodal pelvic radiotherapy (ENRT). The patients were staged with modern molecular imaging, such as PSMA or Choline PET-CT. Eligible patients had detectable pelvic nodal oligo-recurrence ( $\leq 5$  nodes) after radical treatment and were randomized into two arms: arm A received MDT and 6 months of androgen deprivation therapy (ADT), while arm B received ENRT (25 x 1.8 Gy) alongside MDT and 6 months of ADT. The study's primary endpoint was metastasis-free survival (MFS), with secondary endpoints including biochemical relapse-free survival (bRFS) and regional relapse-free survival (rRFS). A total of 196 patients were enrolled. At 3 years arm B demonstrated superior bRFS (69% vs. 47%) and rRFS (90% vs. 70%) compared to arm A, suggesting that ENRT is more effective in preventing relapses in this patient population. Along with the outcomes in terms of efficacy, the trial shows interesting data regarding the risk of toxicity. Genitourinary (GU) side effect rates were higher in the ENRT arm (26% vs 22% at 2 years). Moreover, the MDT arm showed better recovery over time. Interestingly, an in-depth analysis of these specific aspects underlined the impact of previous radiotherapy on the prostate bed or definitive radiotherapy to the prostate to increase the risk of GU toxicity (OR:2.16,  $p=0.03$ ). However, previously irradiated patients showed a significant reduction in pelvic recurrence rates compared to the ones with no previous radiation. This trial supports the use of ENRT plus ADT over MDT in this subset of patients. In my opinion it is very insightful to observe such data using modern imaging (PET-CT), but I believe SBRT still plays a relevant role in

highly selected patient populations, as well as in other settings of PCa.

Another relevant study, the ORATOR trial (2), focused on early T-stage oropharyngeal squamous cell carcinoma (OPSCC), and compared the long-term outcomes of RT versus TORS with neck dissection. A total of 68 patients were randomized, and the primary endpoint was swallowing quality of life (QoL) at one year measured with the MD Anderson Dysphagia Inventory (MDADI). The trial revealed initially higher MDADI scores in the RT arm at 1 year, with a difference of 8 points which was statistically significant but not clinically meaningful as per trial definition. However, by the five-year mark, the scores converged, indicating no significant difference in swallowing QoL between the two treatment modalities. The major differences emerged in the treatment-specific side effects, with a higher rate of pain, trismus, weakness, and cough related to TORS and dry mouth, tinnitus, hearing loss, and neutropenia linked to RT or RT/CT ( $p<0.05$  for each side effect in the analysis). Additionally, overall survival (OS) and progression-free survival (PFS) rates were similar in both groups (5-year OS 84% vs. 85%; PFS 84% vs. 82%), demonstrating that both treatments offer excellent oncologic outcomes with distinct toxicity profiles. Such results, in my perspective, help to clarify and demystify some pre-concepts promoted by media and non-randomized studies regarding the superiority of TORS versus radiation.

In conclusion, the STORM trial highlights the superiority of ENRT with focal RT boost on PET positive nodes over MDT in managing oligorecurrent nodal PCa after primary treatment, at the cost of slightly higher rates of GU toxicity. The ORATOR trial indicates that both RT and TORS provide comparable long-term outcomes for OPSCC with different toxicity profiles. The definition of TORS as superior to RT is not supported by evidence. These findings underscore the importance of individualized treatment approaches based on patient-specific factors, tumor characteristics, and patient preferences. □

Author: Dr. Antonio Angrisani MD, EOC Bellinzona

Mentor: Dr. med. Francesca Caparrotti, Clinique Générale Beaulieu GE

#### References:

1. Salvage Treatment of Oligorecurrent Nodal prostate cancer Metastases (STORM), ESTRO 2024, Abstract 2007
2. Radiation vs Transoral Robotic Surgery for Oropharyngeal Cancer: Final Results of the ORATOR Trial. ESTRO 2024, Abstract 1421