

## Journal Club, November 2025 – January 2026

The November 2025 – January 2026 edition of the **AIROyoung Journal Club** brings together three highly relevant and timely publications that reflect the evolving role of radiation oncology in contemporary multidisciplinary cancer care. Selected from leading international journals, these articles address key clinical and methodological challenges faced by radiation oncologists today: patient selection for metastasis-directed therapy, the safe integration of radiotherapy with modern systemic agents, and the exploration of innovative treatment paradigms in breast cancer.

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**Red Journal**, January 2026

### **Treatment With Stereotactic Ablative Radiotherapy for Patients With Up to 5 Oligometastatic Cancer Lesions: Long-Term Outcomes of the SABR-5 Trial**

Curtis Leclerc, Sarah Baker, Will Jiang, Benjamin Mou, Mitchell Liu, Alana Bergman, Devin Schellenberg, Abraham Alexander, Hannah Carolan, Siavesh Atrchian, Nick Chng, Quinn Matthews, Alexander Benny, Scott Tyldesley, Robert Olson

This population-based, nonrandomized phase II trial reports the long-term outcomes of the SABR-5 study, evaluating stereotactic ablative radiotherapy (SABR) in patients with up to five extracranial oligometastatic lesions treated across six regional cancer centers in British Columbia. Designed at a time when SABR access was limited to clinical trials, the study offers a real-world perspective, with treatment-related toxicity as the primary endpoint and long-term survival outcomes as secondary endpoints.

Between 2016 and 2020, 380 patients were treated, most with one or two lesions and good performance status, including genuine, oligoprogressive and induced oligometastatic disease. With a median follow-up of over 4.5 years, median overall survival was 64.6 months and median progression-free survival 14.6 months; while five-year, overall survival and local control were approximately 60% and 85%, respectively.

On multivariable analysis, poorer performance status, larger tumor burden, lung or colorectal primaries and oligoprogressive disease were independently associated with worse outcomes. In contrast, synchronous and induced oligometastatic disease were not linked to inferior overall survival, suggesting a potential role for SABR beyond the traditional “genuine” oligometastatic setting. Despite the limitations of a single-arm design, this study provides strong long-term population-based evidence supporting the durability and clinical relevance of SABR as metastasis-directed therapy.

**ESMO–ESTRO consensus statements on the safety of combining radiotherapy with CDK4/6, HER2, PARP, or mTOR inhibitors**

Evert S.M. van Aken, Ajeet Kumar Gandhi, Sean M. O’Cathail, Gerben Borst, Jorge Barriuso, Emmanouil Fokasi, Luis Castelo-Branco, Anne Hansen Ree, Evandro de Azambuja, Stephanie Kroeze, Ilaria Colombo, Antonin Levy, Carmen Criscitiello, Maximilian Niyazi, Nadia Harbeck, Ewa Szutowicz, Gabor Liposits, Marcel Verheij, Isabelle Ray-Coquard, Paolo Tarantino, Dario Trapani, Paulien Boot, Claus Belka, Dirk De Ruyscher, George Pentheroudakis, Corrie A.M. Marijnen, Florian Lordick, Umberto Ricardi, Diogo Martins-Branco, Arsela Prelaj, Monique C. de Jong, Bharti Devnani

This joint ESMO–ESTRO project addresses the lack of evidence-based guidance on the safety of combining radiotherapy with modern targeted therapies. Using systematic literature reviews and a multidisciplinary Delphi process, the authors developed tumor-agnostic, scenario-specific safety recommendations for combining radiotherapy with CDK4/6 inhibitors, anti-HER2 monoclonal antibodies, PARP inhibitors, and mTOR inhibitors, based on 107 studies informing 74 clinical scenarios.

The consensus highlights relevant differences among drug classes. Radiotherapy combined with anti-HER2 agents is generally considered safe, with limited need for treatment adaptations, whereas greater caution is recommended for CDK4/6, PARP, and mTOR inhibitors due to their potential radiosensitizing effects and higher toxicity risk in several anatomical sites. Overall, the document provides a pragmatic framework to guide clinical decision-making, emphasizing individualized risk–benefit assessment and the need for prospective studies to strengthen the evidence base.

**ESTRO recommendations on preoperative radiation therapy in breast cancer: current and future perspectives - Endorsed by ASTRO**

Alice Zamagni, Angel Montero Luis, Ingvil Mjaaland, Monica Emilia Chirila, Raquel Ciervide, Melanie Machiels, Ivica Ratoska, Desiree H.J.G. Van Den Bongard, Marianne Aznar, Liesbeth J. Boersma, Charlotte E. Coles, Stefanie Corradini, Alex De Caluwe, Dorota Gabrys, Orit Kaidar-Person, Anna M. Kirby, David Krug, Maja V. Maraldo, Icro Meattini, Sofia Rivera, Navita Somaiah, Vratislav Strnad, Youssef Zeidan, Philip Poortmans

This ESTRO-endorsed paper provides expert-based perspectives on the role of preoperative radiotherapy in breast cancer, an approach that has been explored for decades but has not yet entered routine clinical practice. Based on a structured review of the literature and multidisciplinary consensus, the authors analyze available phase I–II trials across different clinical scenarios, including low-risk early-stage disease, high-risk and locally advanced tumors, and patients requiring mastectomy with breast reconstruction. Overall, existing data suggest that preoperative radiotherapy is feasible and generally safe, with encouraging pathological response rates in selected settings and potential advantages in terms of target delineation, tumor downstaging, and facilitation of breast reconstruction.

However, the evidence base remains heterogeneous and limited, with substantial variability in patient selection, radiotherapy dose and fractionation, timing of surgery, and integration with systemic treatments. As a result, preoperative radiotherapy is considered investigational in most scenarios and

should preferably be delivered within clinical trials. The paper highlights key knowledge gaps and proposes perspectives to guide future research, emphasizing the need for adequately powered randomized studies, standardized reporting of radiotherapy techniques and quality assurance, and the integration of translational endpoints. Overall, this work provides a comprehensive framework to support the design of future trials aimed at defining whether and how preoperative radiotherapy could be incorporated into personalized breast cancer treatment strategies.