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Editorial

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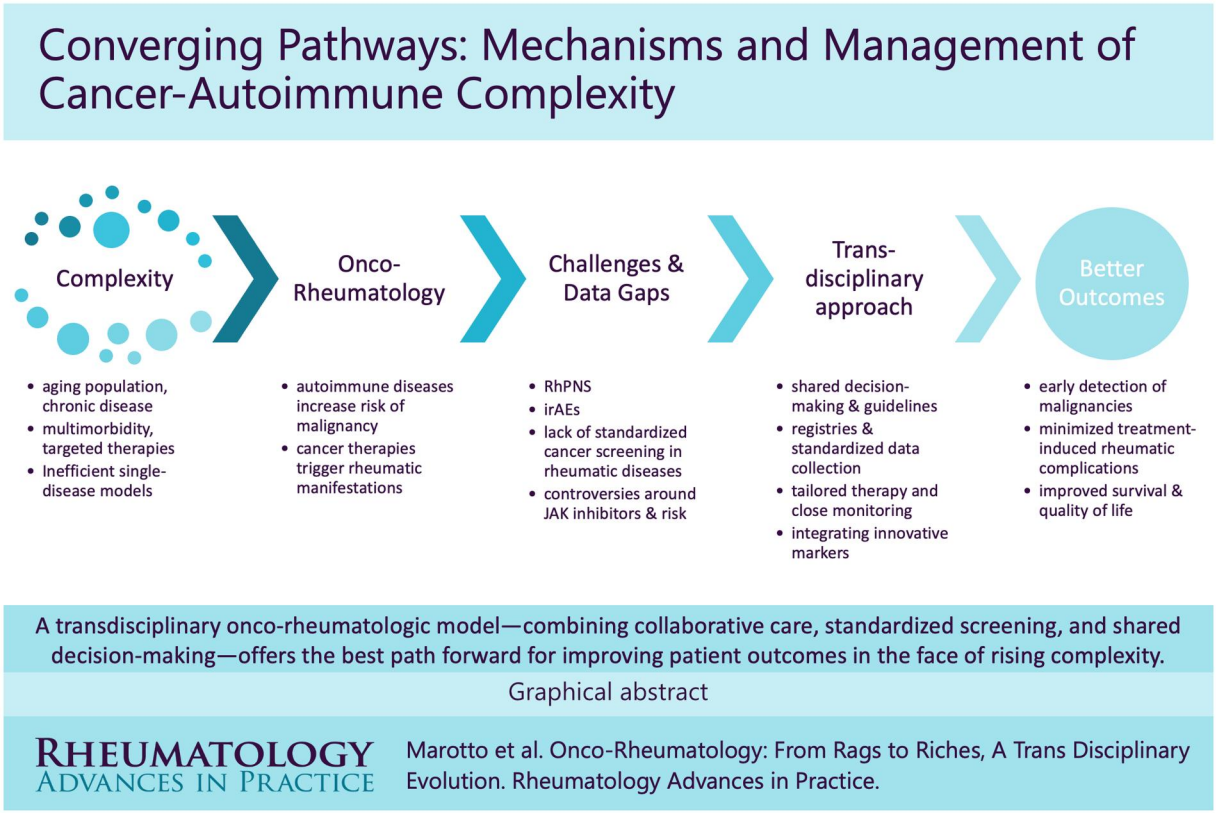
Editorial

Onco-rheumatology: from rags to riches, a transdisciplinary evolution

Graphical abstract



With ongoing advancements in medicine, patient management has become increasingly complex, especially when multiple conditions intersect. The need for integrated, transdisciplinary approaches has never been more critical. This complexity arises not only from the proliferation of targeted therapies, but also from the interplay of multilevel interactions among different organ systems, patient-specific variables and evolving risk factors. In such a non-linear landscape, 'single-disease' models often prove inadequate, as they fail to capture the full scope of intertwined pathophysiological processes. Indeed, the World Health Organization together with the National Institutes of Health and the Italian Ministry of Health advocate for considering the full scope of a patient's life, circumstances and evolving needs rather than the single disease.

Onco-rheumatology, the intersection of oncology and rheumatology, represents a significant complex scientific and clinical challenge that requires urgent attention as central

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questions arise: How can we best manage patients facing overlapping cancer and autoimmune conditions? What are the consequences of treating cancer in the presence of autoimmune diseases, or vice versa? In this rapidly evolving landscape, the EULAR has attempted to address these challenges, but clear data are lacking [1]. The transdisciplinary approach is the solution that emerges from rheumatology's own history in the resolution of systemic sclerosis [2]. The relationship between cancer and rheumatic diseases has been recognized since 1944, with >9000 articles on PubMed exploring the topic, but an integrated onco-rheumatologic model appears in only one paper.

Why does onco-rheumatology matter? The urgency arises from the growing number of patients with autoimmune diseases at higher risk of cancer [3] and the uncertainty about whether new cancer treatments may worsen rheumatic conditions [4]. In addition to the unresolved issues—such as the management of rheumatologic paraneoplastic syndromes and patients undergoing androgen- or oestrogen-suppressive therapy—new challenges have emerged with the introduction of immune checkpoint inhibitors (ICIs). These therapies have revolutionized the treatment of certain malignancies, notably metastatic melanoma and advanced non–small-cell lung cancer, by significantly improving overall survival. Building on these successes, emerging immunotherapeutic strategies such as bispecific T cell engagers (BiTEs) are now under investigation for other tumour types, potentially further expanding therapeutic options. However, ICIs also cause immune-related adverse effects (irAEs) in up to 80% of patients [5]. Within this broader category, rheumatic irAEs (Rh-irAEs) appear in an estimated 5–10% of patients, and while severe cases such as myositis or myocarditis are rare (<1% of patients), their mortality rates can climb to 22%.

These data are also questionable due to the current lack of clarity. First, Rh-irAEs are overshadowed by life-threatening visceral or endocrine irAEs. Second, non-specific symptoms (e.g. arthralgias, myalgias) are misattributed to the underlying malignancy. Third, many Rh-irAEs lack consistent autoantibody markers and exhibit delayed onset. Moreover, prospective trials commonly exclude patients with pre-existing rheumatic disease, and retrospective or real-world studies often group Rh-irAEs together with broader irAEs [4, 5]. Overlapping classifications—for instance, when myositis or myocarditis is labelled simply as an irAE—compound these challenges.

Standardized diagnostic criteria and robust pharmacovigilance with a more systematic strategy are key to enable earlier rheumatologic consultation and tailored treatment, which may include NSAIDs, glucocorticoids, conventional DMARDs, biologic DMARDs or, in certain cases, discontinuation of ICIs [4, 5]. Although epidemiological data indicate higher rates of malignancy in systemic sclerosis, RA, lupus erythematosus and SS [3], no standardized screening protocols currently exist for these populations. Current evidence supports closer surveillance for skin and cervical malignancies in patients receiving immunosuppressive therapy [6], but formal guidelines for lymphoma screening or other cancers remain unclear. This gap underscores the need for ongoing collaboration among rheumatologists, oncologists and primary care teams to establish evidence-based screening strategies.

No studies have evaluated tumour marker–based screening for early neoplasm detection in RA. Innovative approaches such as a multimarker panel (CA125, PSA, CEA, CA19-9, AFP, CA15-3, CA72-4, CYFRA 21-1) combined with artificial intelligence (OncoSeek) have shown 67% accuracy in predicting various cancers in healthy individuals [7]. Another critical issue is the lack of robust data on the impact of rheumatologic therapies on cancer risk. MTX was once believed to elevate cancer risk but no longer appears conclusively linked to higher malignancy rates, biologic DMARDs are similarly unassociated with tumour recurrence or development and rituximab is even recommended for patients with a history of lymphoproliferative disorders.

However, concerns have been raised regarding Janus kinase (JAK) inhibitors. It is true that the introduction of JAK inhibitors has further expanded the options available to rheumatologists, but a recent randomized controlled trial indicated an increased cancer risk (hazard ratio 1.49) in users of tofacitinib, prompting warnings from the US Food and Drug Administration and European Medicines Agency [8]. Safety data have not been clear. Benucci *et al.* [9] found that JAK inhibitors generally have a good safety profile, suggesting that risk factors such as patient age, disease activity, smoking habits and comorbidities also play significant roles in cancer risk. A meta-analysis of 78 clinical trials and long-term studies indicated that JAK inhibitors are not associated with a higher incidence of malignancy compared with placebo or MTX, although a higher incidence is shown compared with TNF inhibitors [1]. Until further evidence emerges, caution and transdisciplinary counselling is advised when prescribing JAK inhibitors to patients with additional cancer risk factors.

The rapid aging of the global population presents another critical challenge, with projections indicating a substantial increase in older age groups by 2050. RA cases peaked in the 75- to 79-year age group in 2020 and are expected to increase by 80% by 2050 [3]. Cancer follows a similar trajectory, with annual cases projected to increase by 77% from the current 20 million new diagnoses and 10 million deaths. Shared risk factors such as smoking, alcohol, infections and pollution contribute to both autoimmune rheumatic diseases and malignancies, with epidemiological data confirming a bidirectional link. In a cohort of 11 262 individuals (2011–2014), cancer patients ($n = 826$) had a significantly higher RA prevalence than those without cancer (9.0% *vs* 3.6%; $P < 0.0001$), with a mean age of 61 *vs* 44 years ($P < 0.0001$) [10].

Managing onco-rheumatologic patients remains a significant challenge due to the complexity of their conditions, which demands a comprehensive transdisciplinary approach. This concept of transdisciplinarity, where knowledge from various disciplines is integrated to create new frameworks, is crucial for addressing their multifaceted needs. The goal is not just achieve short-term results but to ensure long-term patient well-being as their conditions evolve. How can we, as healthcare professionals, ensure these patients receive the comprehensive care they need? Ongoing communication and synergy between specialists are key. This coordinated effort has led to the establishment of the Group of Multidimensional Onco-RhEumatology (G-MORE). It was established as a foundation for onco-rheumatologic collaboration by the Onco-Rheumatology Study Group of the CREI Executive Board (Italian College of Rheumatology) during its 18–20 July 2024 meeting. Its goal is to support scientific societies in further investigating this field and to foster a robust scientific dialogue among physicians. Through this

collaborative approach, we aim to support the advancement of a more integrated, patient-centred care.

Data availability

No new data were generated or analysed for this editorial.

Authors' contributions

D.M., C.M., P.M., A.F., P.A., G.B., G.C., A.F., T.F., F.G., G. I., M.C.M., L.M., L.P. and A.G. all contributed significantly to the work. D.M., C.M., L.P. and A.G. took lead roles in conceptualization, project administration and writing. A.F., P.A. and G.B. were instrumental in reviewing and analysis. G.C., A.F. and T.F. contributed to the methodology and design. F.G., G.I. and M.C.M. provided critical revisions of the manuscript for important intellectual content. L.M., A.G. and L.P. handled supervision and last critical revisions.

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References

1. Sebbag E, Lauper K, Molina-Collada J *et al.* 2024 EULAR points to consider on the initiation of targeted therapies in patients with inflammatory arthritis and a history of cancer. Ann Rheum Dis 2024;ard-2024-225982.
2. Denton CP, De Lorenzis E, Roblin E *et al.* The 2024 British Society for Rheumatology guideline for management of systemic sclerosis. Rheumatology (Oxford) 2024;63:2956–75.
3. Beydon M, Pinto S, De Rycke Y *et al.* Risk of cancer for patients with rheumatoid arthritis versus general population: a national claims database cohort study. Lancet Reg Health Eur 2023; 35:100768.
4. Dang QM, Watanabe R, Shiomi M *et al.* Rheumatic immune-related adverse events due to immune checkpoint inhibitors—a 2023 update. Int J Mol Sci 2023;24:5643.
5. Reynolds KL, Arora S, Elayavilli RK *et al.* Immune-related adverse events associated with immune checkpoint inhibitors: a call to action for collecting and sharing clinical trial and real-world data. J Immunother Cancer 2021;9:e002896.
6. Kedra J, Seror R. Cancer screening in chronic inflammatory rheumatic diseases. Joint Bone Spine 2023;90:105557.
7. Luan Y, Zhong G, Li S *et al.* A panel of seven protein tumour markers for effective and affordable multi-cancer early detection by artificial intelligence: a large-scale and multicentre case–control study. eClinicalMedicine 2023;61:102041.
8. Ytterberg SR, Bhatt DL, Mikuls TR *et al.* Cardiovascular and cancer risk with tofacitinib in rheumatoid arthritis. N Engl J Med 2022;386:316–26.
9. Benucci M, Damiani A, Infantino M *et al.* Cardiovascular safety, cancer and Jak-inhibitors: differences to be highlighted. Pharmacol Res 2022;183:106359.
10. Bhandari B, Basyal B, Sarao MS, Nookala V, Thein Y. Prevalence of cancer in rheumatoid arthritis: epidemiological study based on the National Health and Nutrition Examination Survey (NHANES). Cureus 2020;12:e7870.

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