

inflammatory stimuli. By contrast, Ang2, which is primarily a Tie2 antagonist, binds Tie2 with the same high affinity as Ang1, thereby inhibiting Ang1-induced vascular stability.⁷ The complex interplay between the two includes complementary yet counter-regulatory roles in angiogenesis regulation. That trebananib targets and binds both Ang1 and Ang2 ligands might be a limitation of the drug. Given the considerable cost of bringing drugs to market and restricted resources, a focus on newer methods to enhance success is needed. Deep learning and computational chemistry could represent novel approaches to pharmaceutical research for drug discovery, prioritisation, and toxicity prediction.^{8,9}

It is an exciting time for ovarian cancer, with results anticipated from several potentially practice changing phase 3 randomised trials in the near future. Whether the promise of precision and personalised medicine in ovarian cancer will be realised or the one-size-fits-all approach will yield another negative result remains to be seen.

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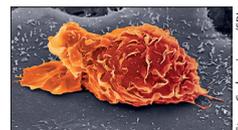
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Multidisciplinary care in tenosynovial giant cell tumours

Tenosynovial giant cell tumour is a rare neoplastic condition of the joint that generally affects patients younger than 40 years.¹ It is not a malignancy per se, but for many, it is far from a benign disease and often causes substantial morbidity and disability due to pain, joint destruction, the need for repeated surgical intervention, and the use of analgesics and narcotics. Although not life-threatening, tenosynovial giant cell tumours can disrupt daily living and adversely alter an individual's life trajectory. Tenosynovial giant cell tumour is a complex disease with a wide breadth of clinical sequelae. Understanding of this disease has changed substantially in the past 10 years after causative genomic events were described.² The discovery of these genomic events has allowed for the development and application of promising therapeutics targeting CSF1 signalling, which are further driving our knowledge base and greatly

informing clinical practice.³ The introduction of CSF1 receptor inhibitors came with the realisation that much needed to be learned about what patients with tenosynovial giant cell tumours go through and how the medical community could best serve them. This realisation prompted the medical and pharmaceutical community to partner with patients, patient advocacy, and patient support groups to learn more about the disease, to develop novel patient-reported outcome measures⁴ and potentially new imaging techniques,⁵ and to review and scrutinise historical experiences.⁵ This effort is paramount because the correct application of targeted therapies in tenosynovial giant cell tumours is not straightforward. Although active, many drugs have serious side-effects and associated financial costs. Much still needs to be learned about appropriate application, patient selection, timing of therapy, and length of use; decisions that need to be



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made in a multidisciplinary fashion, inclusive of the patient and their care team.

Critical to this effort is the data presented in this issue of *The Lancet Oncology* by Monique Mastboom and colleagues⁶ who offer an international, multicentre, retrospective analysis of operable patients with diffuse tenosynovial giant cell tumours. Almost 1200 patients were identified from 31 tertiary care centres and were treated over a 27-year period. The authors provide an invaluable dataset regarding this rare neoplasm of variable clinical behaviour and no defined standard clinical approach to care; specifically, they provide insight into the patterns of surgical practice and outcomes from international centres with expertise in this disease. This insight is critical because the historical treatment for diffuse tenosynovial giant cell tumours is surgical, despite high recurrence rates after surgery of 40–50%.⁶ The infiltrative nature of diffuse tenosynovial giant cell tumours aside, surgical practice is also complicated by the rare nature of this disease and variation in clinical presentations, surgical approaches, and clear and consistent goals of care. This dataset should therefore be instrumental in helping establish uniform guidelines and placing the correct surgical procedures in the context of newer and stronger medical therapies. All of this progress will better serve patients by informing the greater medical and tenosynovial giant cell tumour patient community as to how to approach this challenging disease.

As with any large, multicentre, retrospective dataset that is collected from numerous sites with outcomes and practice patterns spanning several decades, the data is more directional than definitive.⁶ Particularly, in this dataset, practice variation in patient follow-up, compounded by the clinical variation of this disease, leads to imprecision in defining—and ambiguity in interpreting—relapse-free survival. However, the general outcomes are clear, especially for patients initially treated at a tertiary care centre compared with elsewhere. Some practice patterns are also clear—eg, preference of a surgical approach (628 [54%] of 1163 patients had one-staged open synovectomy vs 187 [16%] who had two-staged open synovectomy vs 159 [14%] who had arthroscopic synovectomy)—as is the symptomatic benefit that surgery can afford even when taking into consideration the complex nature of diffuse tenosynovial giant cell tumour symptoms caused

from the disease, joint destruction, or past procedures. In general, when performed in the right patient at centres with experience in diffuse tenosynovial giant cell tumours, surgery remains an important treatment consideration for patients.

Overall, the dataset provided by Mastboom and colleagues will greatly inform the surgical management of diffuse tenosynovial giant cell tumours by directing expert discussions regarding goals of surgery, the best techniques to achieve these goals, the timing of surgery, consistent guidelines for follow-up, and when and how a recurrence should be treated. These data should allow the surgical community to come to a relative consensus regarding standards of care and best surgical practice for diffuse tenosynovial giant cell tumours. Such a consensus would then greatly inform the application of medical management because the intersection and harmonisation of these two modalities provides a very promising horizon for patients who have this very difficult and challenging disease. Efforts can then focus on generating prospective evidence to inform practice.

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