A Surveillance, Epidemiology, and End Results (SEER)-Medicare linkeddatabase analysis showed that the use of chemotherapy was significantly associated with increased risk of fracture and osteoporosis in elderly patients with non-Hodgkin's lymphoma [5].

BMD screening and survivorship evaluation should be part of National Comprehensive Cancer Network (NCCN) and other lymphoma evidence-based medicine guidelines. Preventing bone loss in lymphoma is an important and potentially treatable survivorship issue in these patients.

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disclosure

This trial was funded by Novartis. The data were collected, stored, and analyzed by the investigators alone.

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doi: 10.1093/annonc/mdu044

Rare cancers: work in progress in Europe

Thanks to D. Raghavan for raising the issue of how an 'isolated clinician' should approach rare cancer cases in his editorial to a study on a new regimen for a rare kidney cancer [1]. The outlined steps in management seem very reasonable. I would like to comment on partnerships with experts, pathology review, and methodology of research.

Setting up 'partnerships with experts' at centers of excellence is certainly wise. However, occasional consultations might have limited added value for quality of care, while regular collaborations may be much more effective in the long run. In the end, these are hardly conceivable outside structured health networks. In the European Union (EU), the so-called Cross-Border Healthcare Directive foresees the creation of 'reference networks' especially for rare diseases (http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2011:088:0045:0065:en:PDF). I believe that the European rare cancer community should take up this challenge and look forward to stepping up occasional 'clinical partnerships' to regular 'networks', where lacking. An ongoing initiative named *Rare Cancers Europe*, launched by the *European Society for Medical Oncology* (ESMO) and partnered by many different stakeholders, is trying to address the several problems posed by health networks, also in collaboration with ongoing EU-funded projects, namely RARECARENET (http://www.rarecancerseurope.org/ and http://www.rarecarenet.eu/rarecarenet/).

I strongly agree that centrally reviewing pathologic diagnosis is probably the main step one should make to improve quality of care for any rare cancer patient. However, problems posed by pathology expert opinions in terms of organization of health care and reimbursement throughout EU countries are substantial. In the end, a 'second opinion' cannot be the system answer to a 'frequent' problem (since, as Raghavan recalls, rare cancers are rare individually but not collectively). Recently, *Rare Cancers Europe* hosted a consensus meeting in Brussels, ending at the EU Parliament, to reflect on which rare cancers more deserve pathology centralized diagnoses and to raise the issue of how their referral can be accomplished within the EU countries.

Finally, I fully understand skepticism about isolated case reports, and the like. However, in rare cancers, we need to make the most of all available knowledge, and this goes from anecdotal or quasi-anecdotal observations to controlled trials (including, say, rare cancer international registries or retrospective subgroup analyses within existing clinical trial databases, etc.). Indeed, a lot of theoretical work has been devoted by statisticians to developing new methodologies for clinical research, including Bayesian approaches [2]. How to formally and rigorously sum up all available evidence, whatever its nature, is probably the main challenge. Rare cancers may well lend themselves to serve as a model for methodological innovation, and we, as the rare cancer community, should be more proactive in driving change. *Rare Cancers Europe* is about to release a consensus paper on new methodologies for clinical research into rare cancers. Indeed, rare cancers can be of help in advancing the methodology of clinical research in oncology, at a time when we all are making the point that 'personalized medicine' is turning frequent cancers into groups of rare entities as well.

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disclosure

The author has declared no conflicts of interest.

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